Neurology

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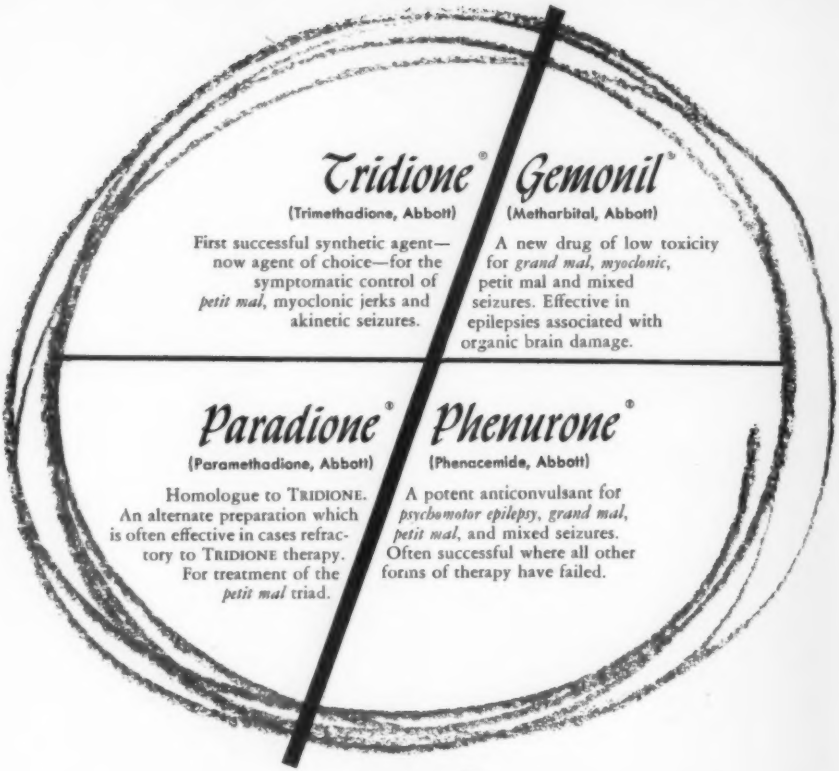
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NEUROLOGY is published monthly at 84 South Tenth Street, Minneapolis 3, Minnesota, by LANCET PUBLICATIONS, INC. Subscription rate: $12.00 a year, $1.00 a copy; outside U.S. $13.00 a year, $1.10 a copy. Entered as second class matter at the postoffice at Minneapolis, Jan. 23, 1951.

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OFFICIAL JOURNAL OF
THE AMERICAN ACADEMY OF NEUROLOGY

Volume 4, Number 2

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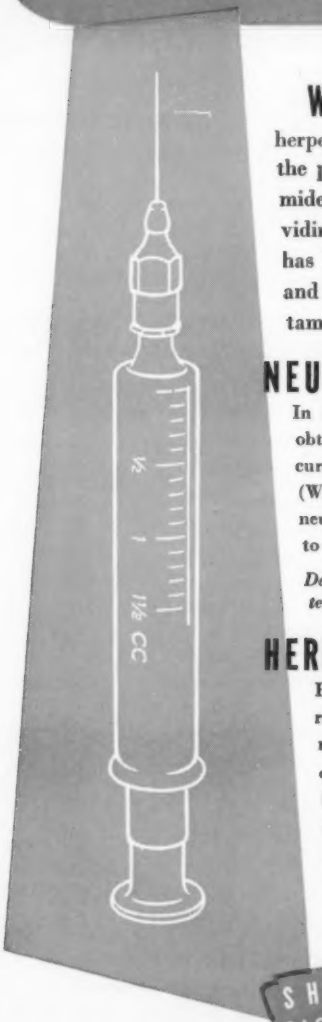

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INFORMATION FOR *Authors*

NEUROLOGY, the official publication of the American Academy of Neurology, has been instituted to provide a medium for prompt publication of articles dealing with neurology and its cognate fields and to stimulate individual investigation in these various fields.

Manuscripts of papers read at meetings of the Academy must be filed with the secretary at the time of the meeting, and will be published if acceptable to the editorial board. They are the property of the Academy, and authors who wish to publish them elsewhere must first request release.

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Neurology

Spontaneous Thrombosis of the Carotid Arteries

Sidney K. Shapiro, M.D. and William T. Peyton, M.D.

THE IMPETUS to the diagnosis of spontaneous thrombosis of the carotid arteries was provided by the introduction of angiography by Egas Moniz[1] and the subsequent report of Moniz and his associates[2] on four cases of nontraumatic thrombosis of the internal carotid artery among 537 patients submitted to angiography. From that time numerous cases have been reported from Germany, Scandinavia, and Portugal and more recently from the United States and Canada. A number of case reports and reviews of this subject are provided in the literature.[3–12] Johnson and Walker[11] were able to record 101 cases from the literature diagnosed by angiogram or open exposure, and to these they added six cases of their own. Antedating the introduction of angiography, the papers of Chiari[13] and Hunt[14] focused attention on this problem. Chiari[13] found that emboli can break away from thrombus material lying in the carotid sinus and cause apoplexy. He observed thrombus deposited on atherosclerotic plaques in the carotid sinus in seven cases in a series of 400 consecutive autopsies. The carotid artery was completely blocked in only one case. Hunt[14] examined the carotid pulsations in 20 cases of hemiplegia and found it absent on the appropriate side in four instances. In addition, the monograph by Hultquist[15] described results of the pathologic study of the entire carotid system in a series of 1300 autopsies.

It is the purpose of this presentation, based upon recorded cases in the literature and our own experience, to outline the clinical features of unilateral spontaneous thrombosis of the carotid arteries. Our series of 17 cases, in which

From the division of neurology and the division of neurosurgery, University of Minnesota Medical School, Minneapolis.

the diagnosis of spontaneous thrombosis of the carotid arteries was established or strongly suggested, will be reported in detail and comment made comparing the features demonstrated by these cases with those recorded in the literature.

SIGNS AND SYMPTOMS

1. *Motor symptoms.* Some degree of muscular weakness is the most common symptom encountered. This may occur first in the hand and arm and later spread to involve the leg, or the upper and lower extremities may be involved simultaneously. Associated with hemiplegia, there may be impairment of consciousness, drowsiness, urinary incontinence, or nocturnal restlessness.

Comment: All the patients in the present series had muscular weakness. In nine patients the initial symptom was muscular weakness, and in the remaining eight paresis developed at some time in the illness.

2. *Headache.* This is a frequently encountered symptom. There is nothing specific about the type of headache in this clinical condition. The headache may be localized to the side of the thrombosis but is frequently generalized. In many instances, it has the characteristic of a migraine headache.

Comment: In only one of the the present series was headache noted (case 2).

3. *Sensory disturbances.* The clinical picture may be ushered in by paresthesias involving the affected side, most frequently in the upper or lower extremities. In association with hemiplegia, there may be objective evidence of sensory disturbance of the cortical type and, in more severe cases, involvement of all sensations.

Comment: In one of the present series (case 13) sensory disturbance was the initial symptom. Six others developed sensory disturbances at some time in their illness.

4. *Aphasia.* Both receptive and expressive aphasias frequently are encountered. These symptoms may antedate all other symptoms or be present in association with a hemiplegia and hemianesthesia. Rarely, aphasia may complicate in right-handed patients on occlusion of the right internal carotid artery.

Comment: Nine patients in this series demonstrated aphasia in association with the motor involvement. In no instance was aphasia present as an only symptom. Of particular interest is case 1 in which aphasia persisted in a right-handed individual in whom the right internal carotid artery was occluded. Andrell[3] (case 5) reported the persistence of aphasia in a right-handed individual in whom occlusion of the right internal carotid artery was demonstrated.

5. *Psychiatric disturbances*. The patient may be a psychiatric problem. In some instances the picture of a psychoneurosis characterized by neurasthenia and anxiety may be present. In others the picture is one of a depression associated with marked deterioration. Some patients are euphoric.

Comment: In case 5 the symptomatology was so vague that an initial diagnosis of a functional disorder was made. The initial symptom noted in case 12 was that of memory loss. In the course of his illness, case 14 developed a change in personality. Slow cerebration and memory difficulty were noted in case 15.

6. *Convulsions.* Convulsions of either a focal or a diffuse type may herald the onset of this condition. Frequently, after the onset of hemiparesis, focal or generalized convulsions may become a part of the clinical picture.

Comment: Convulsions were not encountered in any of the patients in the present series.

7. *Ophthalmologic features.* Patients may complain of episodes of transient blindness early in the course of their illness. At the time of the "stroke," a homonymous hemianopsia may be demonstrated. A primary optic atrophy with visual loss on the side of the involved arteries has been present in a small number of reported cases. More unusual visual symptoms such as diplopia, ptosis, pupillary changes with the ipsilateral pupil being fixed smaller or larger, the presence of papilledema, and paralysis of vertical ocular movements have been reported.

Comment: In four patients (cases 2, 3, 14, 17) visual disturbances ushered in the clinical picture. In two additional patients, visual complaints developed during the course of illness. Cases 16 and 17 deserve special mention in that a primary optic atrophy was visible on the side of the occluded artery. In two instances (cases 2 and 3), the onset of visual complaints was followed by muscular weakness within 12 hours. In case 17 the onset of visual complaints was coincident with the development of a hemiparesis.

8. *Palpation of the carotid and temporal arteries.* This sign has received scant attention in the literature. Its importance has been pointed out previously by Hunt,[14] Webster and co-workers,[9] Fisher,[10] and Johnson and Walker.[11] It should be part of the routine examination. Specific mention of this procedure is omitted in most of the case reports, and further attention to this detail will be necessary before its value can be established.

Comment: In five instances there was a diminution or absence of carotid pulsations on palpation. In one instance, in association with the absent carotid pulsation, there was a decreased pulsation of the temporal and facial arteries on the same side.

9. *Head noises.* Various noises in the head, such as throbbing in the mastoid area, sensation of a watch ticking, a soft roaring in the head, whistle sound in the ear, and a sensation of escaping steam in the ear are complained of by occasional patients.

Comment: In one of our patients (case 11) whistling in the ear was the first symptom noted. Another (case 15) complained of a sensation of escaping steam in the left ear.

10. *Miscellaneous.* Dizziness is a frequent complaint in the reported cases but not described in sufficient detail to enable one to ascertain what the

patient meant by the term. Andrell[3] had a patient with attacks of vertigo so severe that she fell down. One of the reported cases suffered from fits of sneezing.

Comment: Only one of our patients (case 4) complained of dizziness and this symptom was the initial complaint of this patient.

CLINICAL COURSE

Any of the signs and symptoms outlined above may herald the onset of this illness, but the clinical picture may later be complicated by the occurrence of others of the signs and symptoms. The course of this illness follows one of three different patterns.

1. *Transient attacks.* Transient attacks are frequently encountered, characterized by a sudden onset of symptoms which last from a few minutes to an hour and clear either suddenly or gradually. Some residuals of the signs and symptoms may persist until the next attack which may occur days, weeks, or months later. Not infrequently such a series of transient attacks is terminated by a "stroke-like" episode with hemiplegia, aphasia, and sensory disturbances. The term "stuttering" has been used to describe this type of clinical course.

Comment: In ten patients of this series the clinical course was characterized by transient attacks. In two of these (cases 2 and 3) the initial symptom was followed by the development of a hemiplegia within 24 hours. Perhaps these two should be included in the second group, those with an apoplectic type of course.

2. *Sudden apoplectic onset.* Patients in this group may experience, without prior warning, a sudden onset of a hemiplegia which may be associated with severe headache, disturbance of consciousness, urinary incontinence, aphasia, and sensory disturbances.

Comment: Five patients in this series had this type of onset.

3. *Slow progressive course.* This picture closely resembles that encountered in brain tumors in which the clinical course is one of slow gradual progression of symptomatology.

Comment: Two patients in this series demonstrated this type of clinical course. In both, the diagnosis of brain tumor was seriously entertained and ventriculography was performed prior to the establishment of the correct diagnosis.

ANGIOGRAPHIC FINDINGS

Angiography in occlusions of the internal carotid artery may reveal:

1. A conical narrowing of the dye before it stops, resulting in visualization of a stump or short segment of the internal carotid artery (figure 1).

2. Failure to fill the internal carotid artery and a defect or defects in the column of dye produced by the thrombus, extending from the internal carotid artery (figure 2).

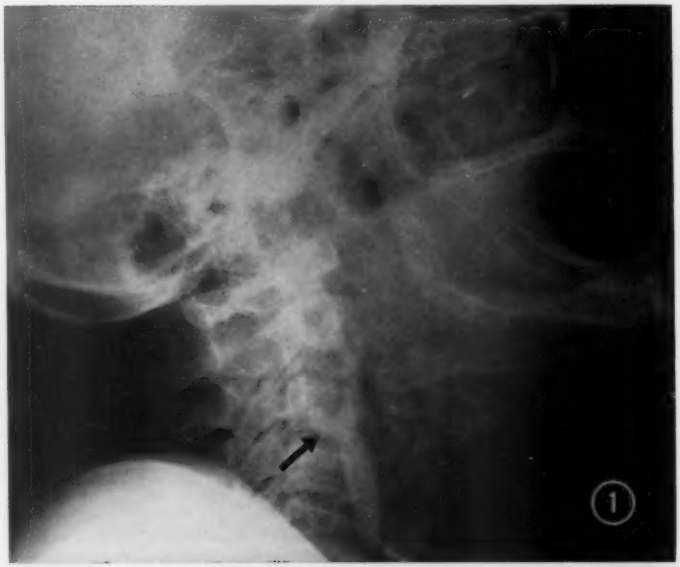

FIG. 1. Angiogram showing conical narrowing of radiopaque dye in the internal carotid artery before it stops. A stump or short segment of the artery is visualized.
FIG. 2. Angiogram showing failure to fill the internal carotid artery, and a defect in the column of dye produced by the thrombus.

3. Retrograde flow of the dye in the common carotid artery and on the right side the flow of dye through the innominate artery into the vertebral artery, resulting in a vertebral angiogram (figure 3).

4. Irregularities in the diameter of the vessel and narrowing of the vessel (figure 4).

5. Failure on repeated attempts to produce any filling of the internal carotid artery.

6. Failure on repeated attempts to produce any filling of the internal carotid artery beyond the carotid siphon.

The first four findings are strong evidence for occlusion of the carotid artery. Where the vessels are narrowed and irregular, a canalization of a thrombus or a partial thrombosis is suggested. Failure to fill the internal carotid artery at its origin after repeated attempts at angiography is suspicious but not diagnostic of internal carotid artery occlusion since it may well be due to technical difficulties. Failure of the carotid artery to fill beyond the carotid siphon likewise must be interpreted with reservation, and such a factor as spasm of the artery must also be considered.

Comment: Eleven patients in this series received angiographic studies, and all examples of the types of findings outlined above were represented in this group of patients. Case 11 deserves special comment in that, following an angiogram performed on the uninvolved side and a pneumoencephalogram performed simultaneously under anesthesia, the patient developed an aphasia upon recovery. Johnson and Walker[11] have pointed out the danger in performing carotid angiography on the side opposite an occluded vessel, and our experience with this one case seems to confirm their observation. Production of a vertebral angiogram in the course of attempting to produce filling of the internal carotid artery, as in case 8, is strongly suggestive of occlusion of the right internal carotid artery. King[16] reported a similar finding in which reflux filling of the vertebral artery took place in a case of occlusion of the internal carotid artery.

ETIOLOGY

The commonest etiology reported in the literature is arteriosclerosis. In this regard atherosclerosis has been described as involving the carotid sinus in the teens and early twenties by Chiari[13] and Keele.[17] Thromboangiitis obliterans has been considered the second most common cause of this condition. Fisher[10] feels that the evidence for thromboangiitis obliterans as recorded in the literature is inconclusive and states, "Further proof is necessary before thromboangiitis obliterans of the carotid and cerebral arteries can be accepted." Other etiologies recorded in the literature include retrograde thrombosis from an intracranial aneurysm and syphilis. Ameli and Ashby[7] mentioned increased viscosity of the blood and polycythemia, temporal arteritis, and polyarteritis nodosa but document no cases of these etiologies. Acute infections have been mentioned, and King and Langworthy[18] described a case

FIG. 3. Angiogram showing retrograde flow of the dye in the common carotid artery, and on the right side the flow of dye through the innominate artery into the vertebral artery, resulting in a vertebral angiogram.

FIG. 4. Angiogram showing irregularities in the diameter of the internal carotid artery and narrowing of the vessel.

of a seven year old boy in whom thrombosis of the right internal carotid artery developed three weeks after pneumonia.

Comment: In 14 of the cases in this series, no etiology for the thrombosis was discovered. Sections of the occluded arteries of six of these patients were studied pathologically, but no conclusion was reached as to etiology. This group of cases would probably be classified in the literature as due to arteriosclerosis. In case 9 a thrombosis of the carotid artery developed during convalescence from pneumonia. Noran, Baker, and Larson[19] present evidence to indicate that there may be intravascular clotting in pneumonia, and such a mechanism could explain the symptomatology in our patient as well as in the patient reported by King and Langworthy.[18] In case 12 the etiology was polycythemia vera; this cause has not been documented in publications regarding spontaneous occlusions of the internal carotid artery. Current publications have very little information regarding studies for the demonstration of blood dyscrasias which might produce an increased tendency to clotting. Further information in this regard is desirable. In case 17 periarteritis was found in other organs of the body at postmortem examination and, although not found in the occluded carotid artery, may have still been an etiologic factor in the production of the occlusion of this vessel. In three patients in this series hypertension was present. Another patient had a history of hypertension, but while under our observation, the pressure was within normal range.

INCIDENCE

This condition affects males preponderantly. There is a predilection for the 30 to 60 age group, although cases ranging in age from 13 to 71 have been reported. There is a definite tendency for the thrombosis to involve the left side more frequently than the right.

Comment: In this series, 14 patients were male and three were female. Two patients were age 35 and 36, respectively. Five patients were between 40 and 50 years of age; six patients were between 50 and 60 years of age; and four patients were between 60 and 70 years of age. In 12 patients the thrombosis occurred on the left side, and in the remaining five on the right side. In 14 patients the internal carotid artery alone was involved. In case 12 the site of thrombosis was the common carotid artery. In case 13, in addition to involvement of the internal carotid artery, there was thrombosis of the common carotid and external carotid arteries. In case 17 obliteration of the ophthalmic artery was present on the involved side in addition to thrombosis of the internal carotid artery.

TREATMENT

In many reported cases no specific treatment was attempted, but in others three forms of therapy have been tried: 1) arteriectomy, 2) cervical sympathectomy, and 3) anticoagulant therapy. This last type of therapy has been used in only a small number of reported cases. The rationale for excision of

a segment of the thrombosed vessel is the belief, by those who used this procedure, that the presence of the thrombosed vessel might result in a reflex spasm of the smaller cerebral vessels and thus account for the transient nature of the symptoms. Against the use of this type of therapy have been the reports in which there is microscopic evidence of recanalization of an old thrombus.

Comment: In six patients of this series (cases 8, 9, 10, 13, 15, 16), a segment of the thrombosed vessel was removed without apparent effect. In case 11, Dicumarol therapy was used for short periods without any apparent improvement, and in this same case repeated stellate blocks following the acute development of aphasia failed to produce any relief of this symptom. In case 8, the patient showed marked improvement while receiving Dicumarol. Neurologic rehabilitation is indicated as nonspecific therapy.

PROGNOSIS

The prognosis for improvement following establishment of the diagnosis is not particularly hopeful. Twenty-five per cent of the cases studied by Johnson and Walker[11] showed some improvement with or without treatment. There seems to be no correlation between the degree of involvement and the type of onset. Thirteen of the patients reviewed by Johnson and Walker[11] died within several months after onset.

Comment: Two patients (cases 12 and 17) of the present series have died.

VENTRICULOGRAPHY AND PNEUMOENCEPHALOGRAPHY

The characteristic picture following air studies is that of dilatation of the ventricles, particularly on the involved side. A brain tumor may be present in addition to thrombosis of the carotid arteries, and some suggest air studies in addition to angiography.

Comment: In cases 5 and 15, ventriculography revealed no abnormalities. In case 11 a pneumoencephalogram was normal.

CASE REPORTS

Case 1.—A 46 year old white man was in good health until August 23, 1952. At that time he was approached by a game warden while fishing and suddenly became unconscious. He remained totally unresponsive for the next week. Examination on August 30 showed the following findings: The patient was unresponsive except to painful stimuli, which produced movement of the right side of the body but not of the left arm or leg. A left lower facial paralysis was present. The deep reflexes on the left could not be elicited and there was a questionable Babinski on the left. The patient was unresponsive to painful stimulation on the left side of the body. On funduscopic examination the vessels in the right fundus appeared very narrow with what appeared to be decreased blood in them. The disks were normal. On palpation of the carotid arteries in the neck, that on the right felt firm with a minimal pulsation. A percutaneous angiogram on September 11 demonstrated a complete occlusion of the right internal carotid artery at its origin.

The patient showed gradual improvement. Over a period of several weeks he became more alert and carried out commands, but he was unable to talk and had difficulty eating. The patient had always been right-handed. Paralysis of the left arm and leg remained complete, and the deep tendon reflexes on the left became more active than those on the

right. The Babinski on the left was positive. No appreciation of sensation was demonstrable in the paralyzed extremities.

Comment: This patient had the sudden apoplectic onset of his clinical symptomatology. The diagnosis of internal carotid artery occlusion was suspected after palpation of the carotid arteries which revealed a firm artery with minimal pulsation on the right. It was proved by the angiogram which showed complete occlusion of the right internal carotid artery at its origin. Of interest is the persistence of speech disturbance in this patient.

Case 2.—A 41 year old white man was admitted on August 20, 1952 for investigation of his complaints of blurred vision and a previous history of right-sided weakness. He had been in perfect health until June 25, 1952 when he developed a transient blurring of vision in the morning. That evening he experienced difficulty manipulating change in his pocket, dropped some, and fell when bending over to pick up the coins. He was unable to move his right upper and lower extremity and his speech was not intelligible. There was no loss of consciousness. The following morning he was able to move the extremities and speak more clearly, and improved rapidly over the next week. In another week, he stated that strength in his right extremities had returned to normal. He returned to work, but had another episode of blurred vision on August 6. The next morning he experienced a fainting sensation. Examination revealed the following positive findings: The general physical examination was negative. The systolic blood pressure was 134 and the diastolic 86. The deep tendon reflexes in the right upper extremity were greater than those in the left. The Oppenheim and Gordon signs on the right were questionable. The left ankle jerk was more active than that on the right. No evidence of paresis could be demonstrated.

A left carotid angiogram done under local anesthesia showed occlusion of the left internal carotid artery 1 cm. from its origin.

Comment: This patient had one transient attack of visual disturbance followed within a matter of hours by apoplectic onset of weakness. He made a rapid recovery from this initial episode, but subsequently had one more bout of visual disturbance. The diagnosis of internal carotid artery occlusion was proved by angiogram.

Case 3.—A 35 year old white man was admitted to hospital on August 25, 1952. Thirteen days prior to admission he developed transient blindness in the right eye of five minutes' duration. The next morning he noted a right-sided paralysis upon awakening and complained of a severe headache. Examination at that time revealed a right hemiplegia, aphasia, and a right homonymous hemianopsia. The headache lasted about four days and has not reappeared since. The right hemiparesis and aphasia gradually improved.

At the time of his hospital admission the examination revealed the following positive findings: There was a mild right hemiparesis and a mild right lower facial paralysis. The deep tendon reflexes were hyperactive on the right side. An expressive aphasia was present. The right hemianopsia previously present had disappeared and there was only a mild field defect on the right side.

Routine blood and urine studies were normal. The serology was negative. Radioactive isotope encephalometry was normal. The blood pressure was 115/70. On August 26 a left carotid angiogram showed a very incompletely-filled, somewhat ragged appearing internal carotid artery, especially in the region of the carotid siphon. The appearance was compatible with a partial thrombosis of the carotid artery. There was a minimal filling of some of the branches of the posterior cerebral artery, and on the latter films, the internal cerebral vein and the basal vein. The vein of Galen was filled with some contrast medium as was also the straight sinus. There was no visualization of the anterior and middle cerebral arteries on any of the films.

Comment: The clinical picture and angiographic findings suggest a diagnosis of probable thrombosis of the internal carotid artery. Interpretation of failure of the carotid artery to fill beyond the carotid siphon must be made with caution. The radiologic picture suggested a partial thrombosis of the carotid artery since some of the contrast medium passed

into the posterior cerebral artery and subsequently into the veins. Radioactive isotope encephalometry revealed no abnormality.

Case 4.—A white woman about 50 years old was admitted to the hospital on May 11, 1950. On the day of admission she had developed an acute episode of dizziness. Routine blood and urine studies were negative. The serology was negative. Examination revealed the following positive findings: The systolic blood pressure was 165 and the diastolic, 95. The neurologic examination was negative. On palpation of the carotid arteries it was found that there was no pulsation in the left internal carotid artery, which was cord-like and could be rolled beneath the examiner's fingers.

The patient's dizziness cleared in six months and she was asymptomatic until April 1951 when weakness developed in the right upper extremity. Coincident with this, she complained of headaches and lack of energy. In June there was a recurrence of the dizziness, and seven days after its onset reexamination showed the blood pressure the same as it was a month previous. There was a mild right hemiparesis, most marked in the right upper extremity, accompanied by a mild right lower facial paralysis and a mild right-sided hyperreflexia. The occluded artery previously palpated had not changed.

Comment: The diagnosis of occlusion of the left internal carotid artery is strongly suggested by the palpation of this vessel which revealed absence of any pulsation and a cord-like character of the vessel. This case is best classified under those in which transient attacks are characteristic.

Case 5.—A 51 year old white man was admitted to the hospital on July 16, 1952. He had first been seen six days previously. There was a three month history of unusual involvement of the legs and arms. This condition consisted of some incoordination and a sensation that the affected extremity was asleep. The left lower extremity was initially involved, but subsequently the other three extremities were affected. These peculiar attacks lasted from a few minutes to half an hour. During the last episode which involved only his legs, the patient stated he was so unsteady he could not walk. The neurologic examination was completely negative and a diagnosis of a functional disorder was made.

Two days later the patient became drowsy and confused and experienced difficulty with speech and gait. At the time of admission he was not sufficiently responsive to give any history. At this time the neurologic findings were still minimal although there now appeared to be some weakness of the right side with slight right hyporeflexia. At times the patient appeared to be definitely aphasic, but this was difficult to assess because of the general mental status. A spinal puncture revealed a pressure of 280 mm. of water. The possibility of a brain tumor was seriously considered and a ventriculogram was performed, but it was entirely negative.

Two attempts to perform a carotid angiogram failed to produce filling of the internal carotid system on the left. On August 16 an open angiogram was performed. The internal carotid artery on the left did not fill and there was a retrograde flow of dye in the common carotid artery. Routine blood and urine studies, radioactive isotope encephalometry, serology, and a biopsy of the cortex at the time of the ventriculogram were negative.

Comment: The bizarre nature of the presenting complaints with involvement of all extremities and absence of any neurologic findings initially suggested the diagnosis of a functional condition. The subsequent development of organic symptomatology and findings plus increased spinal fluid pressure led to serious consideration of a diagnosis of brain tumor. The demonstration of complete occlusion of the left internal carotid artery by repeated angiography finally established the diagnosis. This case is probably best classified among those which have a slow progressive course simulating brain tumors.

Case 6.—A 60 year old white man was admitted to the hospital on February 12, 1952. About two years prior to hospital admission this patient had a sudden onset of weakness of the right arm and leg without loss of consciousness. This weakness cleared in two days. One year prior to admission to the hospital, he again developed weakness of the right leg

which cleared in several days. On February 5 a loss of speech suddenly developed. He understood everything that was spoken to him and could read, but he was unable to write. This began to clear on the fifth day and continued to improve up to the time of the patient's admission to the hospital.

The general physical examination revealed a systolic blood pressure of 164 and a diastolic of 100. On palpation of the carotid arteries the right carotid pulsated well. On the left the internal carotid artery pulsated less strongly and felt smaller in caliber. The examiner estimated that it was about half the size of the artery on the right. The patient complained of some subective difficulty with speech, but this could not be demonstrated objectively. He fell to the right on tandem walking. The remainder of the neurologic examination was negative.

Routine blood and urine studies and serology were negative. The bleeding and clotting times were normal, as were the chest and skull.

Comment: The clinical picture and the decrease in pulsation of the left internal carotid artery suggest the diagnosis of partial occlusion of the left internal carotid artery. This case falls into the group of cases characterized by transient attacks.

Case 7.—A 60 year old female Indian was admitted to the hospital on February 22, 1952. She had a history of hypertension of four to five years' duration. In 1948 three left-sided strokes occurred without loss of consciousness. Following the first two strokes there were no residuals and recovery was complete. Following the third episode there had been residual paresis and spasticity on the left. In January 1952 there was sudden onset of slurring of speech and further weakness of the left arm and leg. Since that time she has had marked weakness of the left arm and to a lesser extent the left leg.

On admission the blood pressure was 134/88. Palpation indicated that the carotid arteries in the neck were normal. The remainder of the general physical examination was negative. The positive findings on the neurologic examination were as follows: left hemiparesis with spasticity; subjective hemihypesthesia on the left and the position sense mildly reduced in the left upper and lower extremities; hyperreflexia, positive toe signs, and a sustained ankle clonus present on the left.

Visual fields were within normal limits. Routine urine and blood studies were normal. The Wassermann was negative. The bleeding, clotting, and prothrombin times were normal. The electroencephalogram was abnormal with a diffuse dysrhythmia but no focalization. Radioactive isotope encephalometry showed a focus in the right posterior fossa.

On February 28 a right carotid angiogram was performed and only the external carotid was visualized. On March 4 the angiogram was repeated. The common carotid and the external carotid on the right were filled and most likely normal. The internal carotid ended bluntly 1 cm. from the bifurcation and a diagnosis of occlusion of the internal carotid artery was made.

Comment: This patient's clinical course was characterized by transient attacks of paralysis, finally resulting in some permanent paralysis. The angiogram was diagnostic and established the diagnosis of occlusion of the internal carotid artery. A radioactive uptake study showed a focus in the right posterior fossa.

Case 8.—A 51 year old farmer was admitted to the hospital on July 29, 1950. He had been in good health until November 1949 when he developed transient bouts of flaccid paralysis of the left leg. He began to note similar attacks involving the left arm about January 1950. The leg and arm attacks might occur separately or together and varied in duration from ten minutes to two hours. These attacks usually occurred at intervals of several days, but on one occasion a two month period elapsed without any symptoms. During the attacks in which the arm was involved, the patient was unable to move the arm unless he yawned. While yawning he was able to raise the left arm. Three weeks prior to hospital admission some numbness and tingling of the left lower face and some difficulty with speech was noted. At the time of admission the blood pressure was 160/90. There was a left-sided hemiparesis. Astereognosis, decrease in vibration sense, and a slight

decrease in position sense were demonstrated in the left upper extremity. There was a mild left hyperreflexia. There was an unsustained left ankle clonus. Roentgenograms of the skull, routine blood and urine studies, and the blood Wassermann were negative.

Bilateral angiograms were performed on August 2. On the left there was good filling of the internal carotid artery, the anterior and middle cerebral arteries, and their branches. When the left angiogram was performed there was also some filling of the right anterior cerebral artery. On the right there was no filling of the right internal carotid artery. There was considerable filling of the right external carotid artery and its main branches. Excellent filling of the vertebral artery on the right was obtained. On August 3 the angiogram was repeated on the right side and exactly the same results were obtained as from the previous right carotid angiogram. On August 7 the right internal carotid artery was explored. The common carotid artery was large. There was ecchymosis about it and it was very adherent to the surrounding tissues. This condition of the artery extended up to the bifurcation and through the bulb and it was the opinion of the surgeon that this reaction was due to the previous angiograms. There was good pulsation in the common carotid and external carotid artery. The internal carotid artery was exposed for a distance of about 2 cm. above the bifurcation and it did not pulsate. Aspiration of the internal carotid artery failed to reveal the presence of any liquid blood. A 1 cm. segment of the internal carotid artery was excised and examined pathologically.

The patient was started on Dicumarol therapy and remained on it until May 7, 1951. At this time his condition was reassessed. Following discharge from the hospital there had been gradual improvement in motor weakness. At the time of readmission, the chief weakness remained in the finger movements of the left hand only. Curiously enough, in spite of Dicumarol therapy and maintenance of the prothrombin time around 50 seconds, the patient developed a coronary thrombosis which necessitated hospitalization for two weeks.

Examination following readmission on May 7 revealed a blood pressure of 190/110. The patient was alert and cooperative. There was some edema of the left hand, with paresis of the muscles of the left hand and of the left wrist. The rest of the musculature was intact. The deep reflexes were all hyperactive, moreso in the left upper extremity. Slight involvement of deep sensation remained in the left upper extremity but this also showed marked improvement. Laboratory studies were all within normal limits. Because of the patient's remarkable improvement it was felt that no further Dicumarol therapy was indicated and the drug was discontinued.

Comment: This patient's clinical course was characterized by transient attacks of weakness involving the left arm and leg. There was an associated disturbance of deep sensation in the upper extremity. The diagnosis of thrombosis of the internal carotid artery was proved at surgery. Following institution of Dicumarol therapy the patient made a remarkable recovery, but while on this therapy a coronary thrombosis developed.

Case 9.—A 48 year old white woman was hospitalized on February 1, 1952 for investigation of left-sided weakness. In July 1951 she developed bilateral pneumonia for which she was hospitalized. During convalescence, on approximately the tenth day of illness, a sudden left hemiparesis developed associated with mental confusion. There was a gap in memory for approximately two weeks but there was no definite history of coma. Pain in the joints of the left extremities developed soon after onset of paresis. The paralysis and left-sided pain which developed eight months before admission remained.

Examination showed an obese disheveled woman. The patient was alert but uncooperative and evidenced excessive suspicion. The carotid arteries were palpable bilaterally. The abnormal neurologic findings were limited to the left side and included hyperactive deep reflexes, absent abdominal reflexes, unsustained knee clonus, sustained ankle clonus, positive toe signs, rigid extremities with spasticity and possible ankylosis, hemihypesthesia, decreased stereognosis, and decreased position sense. The blood pressure was 130/80.

Routine blood and urine studies were negative. The blood Wassermann was negative.

Roentgenograms of the skull and chest were negative. Radioactive isotope encephalometry showed a diffuse increase on the right with varying percentage differences but no focus.

On February 6 a right carotid angiogram failed to visualize the internal carotid artery on this side. On March 3 the right common carotid artery was explored. The bifurcation was found and no pulsation could be seen or felt in the internal carotid artery. The external carotid artery appeared to be normal and there was a good pulse. The internal carotid was ligated about 2 cm. above the bifurcation and a section of the artery was taken and examined pathologically.

Comment: This patient had an apoplectic type of onset of symptoms and has as residuals a left-sided hemiparesis and left-sided sensory findings. This case is of particular interest since the onset of symptoms occurred during convalescence from pneumonia. The diagnosis was established by the absence of filling of the internal carotid artery on angiogram and by subsequent surgical exposure and excision of a segment of the thrombosed artery. Radioactive isotope encephalometry showed a diffuse increase on the involved side with varying percentage differences but no focus.

Case 10.—A 52 year old white man was admitted to the hospital on February 4, 1952. On the day prior to admission this patient fell and struck the left side of his head. Following this injury blood was noted on the head but the source was not determined.

At the time of hospital admission the patient was semicomatose and it was noted that he was unable to move the right side of his body. Respirations were irregular. The pulse and blood pressure were within normal limits. Examination of the fundi was negative. There were a right hyperreflexia and positive toe signs on the right. As the patient's state of consciousness improved, a right hemihypesthesia and a right homonymous hemianopsia were suspected. A spinal fluid examination was done with negative results. Because of the disturbance of consciousness and the focal neurologic findings, a dural hematoma was suspected and trephines were performed with negative results. The state of consciousness improved steadily and by February 8 the patient was alert and followed simple directions, but had some difficulty understanding and could not speak coherently. Three attempts at angiography were made on the left. On the first two attempts the external carotid artery alone showed filling. On the third attempt, in addition to the filling of the external carotid and its branches, only the initial few centimeters of the internal carotid artery filled. An exploration of the internal carotid artery in the neck was performed and a thrombosed vessel was found. A section of this vessel was removed for pathologic examination. The patient continued to improve gradually and was ambulatory at the time of his discharge on March 18. A mixed aphasia persisted. The routine blood and urine studies were negative. The hematocrit on three occasions was 50.5, 51, and 47. The hemoglobin was reported as 17.5, 18.4, and 16.6. The routine serology was negative.

Comment: This patient demonstrated an apoplectic type of onset of symptomatology. Trephines were performed with negative results. The diagnosis of occlusion of the internal carotid artery was established by angiography and subsequent operative intervention.

Case 11.—A 48 year old white man was admitted to the hospital on January 23, 1950. His complaints dated from eight weeks prior to admission. At that time he began to hear a whistle in the ear synchronous with his heart beat. Two weeks later intermittent numbness in the right arm and leg were noted, and at about the same time he noted difficulty in using the right arm and leg. On January 10 he noted stiffness in the neck and at the same time the numbness in the right side became constant. The positive findings on examination were incoordination of the right arm and to a lesser extent, the right leg. There was a mild hyperreflexia involving the deep reflexes on the right.

Repeated attempts at closed angiography on the left failed to produce visualization of the internal carotid artery. Finally an open angiogram was done and the needle was directed downward into the common carotid artery below the bifurcation; again no filling of the internal carotid artery was produced. The diagnosis of thrombosis of the internal carotid artery on the left was made. Dicumarol was administered until February 11 with-

out progression of symptoms and the buzzing in the ears disappeared. Before discharge a right-sided angiogram and a pneumoencephalogram were done to rule out the possibility of a tumor. Dicumarol was discontinued prior to these procedures. Both procedures were performed at the same time under general anesthesia. When the patient regained consciousness an aphasia had developed. He was again put on Dicumarol and showed slight improvement in that he was able to say a few words. The aphasia was mostly motor and there was apraxia causing agraphia. Repeated stellate blocks were performed after the patient developed aphasia, but they did not influence his condition materially. Routine skull roentgenograms, blood and urine studies, and the Wassermann were negative. Clotting time and protein in the spinal fluid were normal. The right cerebral angiogram and pneumoencephalogram performed on February 11 were normal.

A follow-up report received from a friend of the patient in May 1952 indicated that there had been a progression in his aphasia, and that he had become unable to speak. His handwriting had become unreadable.

Comment: The symptomatology of this man's condition was ushered in by auditory manifestations. Since the course of illness was slow and progressive a brain tumor was considered a definite possibility, so an angiogram on the normal side and a pneumoencephalogram were performed. Following these procedures, which were done simultaneously under anesthesia, the patient developed an aphasia. He received Dicumarol therapy with slight initial improvement. The diagnosis of occlusion of the left internal carotid artery was established by repeated angiography.

Case 12.—A 36 year old white man developed a moderately severe headache on August 10, 1948, continuing for several days. On August 15 he noted nausea and vomiting and became lethargic. He was hospitalized the following day when he lost the ability to talk or use the right arm. Past history revealed that he had had mild but definite memory loss for several months and had complained of numbness in his hands on several occasions. Two years previously he had experienced an episode of ankle edema and was told he had "kidney disease." Examination revealed an expressive and receptive aphasia, weakness of the right arm and lower face, and hyperactive reflexes on the right. Physical examination showed enlargement of the spleen. The hemoglobin was 18 gm.; red blood count, 6,360,000 per cu. mm.; hematocrit, 56.5 per cent. The clinical diagnosis of polycythemia vera was made and treatment in the form of venesection was instituted.

A few days after admission the patient grew more alert and began to understand simple statements. He improved gradually and was beginning to talk. However, eight days after admission aphasia became complete and weakness of the right leg developed. At this time no pulsation of the left carotid artery could be detected. The patient again began to improve but two weeks later developed a pulmonary infarct. Three months later death occurred following a thrombosis of the superior mesenteric artery.

Comment: This patient's illness had a slow progressive course. This case is of particular interest since the cause of the thrombosis of the common carotid artery was polycythemia vera. This condition has not been implicated in recent publications concerning the etiology of spontaneous occlusion of the carotid arteries. Postmortem examination showed complete occlusion of the left common carotid artery.

Case 13.—A 65 year old white man was admitted to the hospital on August 13, 1951. He complained of periodic episodes of numbness in the right arm and leg of four months' duration. These episodes occurred when raising the head (as when drinking water). Two months prior to admission he had an episode of expressive aphasia and subsequent to this had several similar episodes. One month prior to admission he sustained a weakness of the right leg which lasted about one hour. Subsequently, two similar episodes of weakness occurred. The general physical examination revealed an absence of carotid pulsations on the left. Pressure over the left carotid sinus caused this patient to complain of the numbness which he had experienced in the attacks. The neurologic examination failed to reveal any abnormalities. The systolic blood pressure was 120 and the diastolic, 80.

Roentgenograms of the skull and chest, a barium enema, and an esophagogram were all negative. The electrocardiogram was normal. The routine blood count was normal. Urinalysis showed 30 to 35 white blood cells. On August 21 the left common carotid artery was explored. It was found to be completely occluded by a thrombus which extended to involve the internal and external carotid arteries. The common carotid artery was opened and there was no bleeding. A segment of the common carotid in continuity with the proximal parts of the external and internal carotid arteries was excised.

Comment: This patient's condition was characterized by transient attacks of numbness, weakness, and aphasia. Of particular interest was the finding that palpation of the carotid sinus on the involved side reproduced his sensory complaints. Clinically there was an absence of carotid pulsations on the left, and the diagnosis of thrombosis of the common, internal, and external carotid arteries on the left was proved at surgery.

Case 14.—A 51 year old white man was admitted to the hospital on September 11, 1952. In the summer of 1952 he began to have visual disturbances which he described as attacks of "blackness." At first these lasted 30 minutes and occurred about once a day. Coincident with the onset of visual complaints the patient developed a change in personality manifested by forgetfulness and inability to initiate activity or direct his business. The visual symptoms increased in severity and duration. Upon awakening on September 1 he was found to have developed an aphasia, right hemiplegia, and right homonymous hemianopsia. He spent the next five weeks in bed and there was a gradual improvement in the motor weakness and the aphasia. The positive findings on admission were a mixed aphasia and, on the right side, a homonymous hemianopsia, hemiparesis, hyperreflexia, and positive toe signs. The carotid arteries were palpable in the neck. The systolic blood pressure was 135 and the diastolic, 85. Radioactive uptake studies revealed an abnormal record with a high uptake in the posterior areas, moreso on the left. Routine blood and urine studies and the Wassermann were negative.

A left carotid angiogram was performed on two occasions. In both instances the external carotid branches were well visualized. The internal carotid artery was definitely narrowed and was not visualized beyond the region of the sella turcica.

Comment: This man's clinical picture was characterized at onset by personality changes and transient attacks of visual disturbance. He subsequently developed a hemiplegia with an associated aphasia and homonymous hemianopsia. The angiogram suggested occlusion of the internal carotid artery on the left. The internal carotid artery was definitely narrowed and was not visualized beyond the region of the sella turcica. The diagnosis in this case was probable thrombosis of the internal carotid artery. Radioactive encephalometry revealed abnormalities.

Case 15.—A 56 year old white man was first seen in January 1951. It was difficult to obtain an accurate history from the patient. As far as could be ascertained he injured his right knee in 1940 and had difficulty walking for a while. Since 1947 the patient had complained of clumsiness in the right lower extremity and this had progressed to involve the left lower extremity. During the four year period prior to examination he had also complained of various pains throughout the body, particularly in the chest, and vague sensory disturbances involving the left lower extremity and the right abdominal wall. During this same period auditory complaints consisted of a constant rushing escaping steam sound in the left ear. In December 1950 the patient developed difficulty in writing and talking.

At the time of the initial examination the neurologic findings were normal except for slow cerebration, a mild right hyperreflexia, and a positive Babinski on the right. The patient was admitted to the hospital on February 28. At this time his difficulty with memory and mentation generally had clearly progressed. The neurologic findings remained unchanged. Routine blood and urine studies were negative. The systolic blood pressure was 140 and the diastolic, 80. The serology was negative. A ventriculogram was normal.

Two angiograms on the left side failed to fill the internal carotid artery. On March 10, 1951 an open angiogram was done and a thrombosis of the internal carotid artery was

discovered. A segment of the internal carotid artery was excised just above the bifurcation and examined pathologically.

Comment: This patient falls into the group characterized by progressive symptomatology. During the early stages of illness, there were auditory complaints. In addition vague complaints of clumsiness involving the lower extremities, various pains throughout the body, and vague sensory disturbances were also present. After repeated angiography failed to produce filling of the internal carotid artery, the neck was explored and a diagnosis of thrombosis of the internal carotid artery was made. A segment of this artery was excised. A ventriculogram done prior to angiography was normal.

Case 16.—A 43 year old white man was admitted to the hospital on January 22, 1951. Four months prior to hospital admission he had sudden onset of aphasia and a right hemiplegia.

At the time of admission to the hospital the systolic blood pressure was 90 and the diastolic, 60. There was no pulsation palpable in the common or internal carotid arteries on the left. There was absence of pulsation of the left temporal artery, while the corresponding artery on the right demonstrated excellent pulsation. The facial artery on the left pulsated weakly in comparison with that on the right. The neurologic examination revealed a primary optic atrophy on the left with very tenuous arterioles in the left retina, right hemiparesis, hyperreflexia, positive toe signs, and a mixed aphasia. The patient was totally blind in the left eye.

Routine blood and urine studies were negative. Electrocardiograms, esophagograms, and skull roentgenograms were normal. The right angiogram was normal. The serology was negative.

On February 15 the left common carotid, external, and internal carotid arteries were exposed at operation. No pulsations were seen in the common carotid artery, in the carotid bulb, or in the internal carotid artery. The external carotid artery was pulsating and branches of ascending pharyngeal and the superior thyroid arteries were all pulsating well, probably from collateral circulation in the neck through the branches. The internal carotid artery was then sectioned above the bifurcation and found to be completely thrombosed. A large segment of the internal carotid artery in its wall was then taken out to effect periarterial sympathectomy and for biopsy.

Comment: This patient had an apoplectic onset of symptomatology. Absence of pulsation of the carotid artery and decreased pulsation of the temporal and facial arteries on the same side were noted. The diagnosis of occlusion of the common carotid and internal carotid arteries was proved at operation and a section of the internal carotid artery was removed. Of particular interest were blindness and a primary optic atrophy on the side of the occluded arteries.

Case 17.—A 68 year old white man was admitted to the hospital on August 2, 1951. In 1943 this patient had experienced suddenly left-sided weakness associated with marked diminution of vision in the right eye. The weakness gradually improved and cleared in one month. Diminution of vision persisted. At the time of the last hospital admission the patient was markedly cachectic and expressed the desire to die.

The routine blood and urine studies were negative, as was the blood serology. Systolic blood pressure was 110/80. The neurologic examination was negative except for a primary optic atrophy in the right eye with which he could distinguish only fingers.

Suddenly on September 22 the patient became semicomatose and rapidly lapsed into coma. At this time examination revealed conjugate deviation of the eyes to the left, right primary optic atrophy, and increased left ankle jerk. A tentative diagnosis of right internal carotid artery occlusion was made. The patient's condition deteriorated rapidly and he died on September 25.

Postmortem examination showed periarteritis nodosa with involvement chiefly of the kidneys, muscle, adrenal glands, spleen, and bladder. No evidence of periarteritis nodosa

was discovered in the internal carotid artery. The right ophthalmic artery was seen only as a thin fibrous band.

Comment: This patient had an apoplectic type of onset of illness. Of interest are the persistence of visual difficulty and demonstration of a primary optic atrophy in the involved eye. Eight years after the initial episode the patient suddenly lapsed into coma and died several days later. Of interest is the demonstration of periarteritis nodosa in the organs of the body other than the carotid arteries and the nervous system. The thrombosis of the right internal carotid artery and obliteration of the right ophthalmic artery were present at post mortem. The encephalomalacia was in the distribution of the right middle cerebral artery.

REFERENCES

1. Moniz, Egas: L'encephalographie arterielle, son importance dans la localisation des tumeurs cerebrales, Rev. neurol. 2:72, 1927.
2. Moniz, Egas, Lima, Almeida, and De Lacerda, R.: Hemiplegies par thrombose de la carotide interne, Presse méd. 45:977, 1937.
3. Andrell, O.: Thrombosis of the internal carotid artery; A clinical study of nine cases diagnosed by arteriography, Acta med. scandinav. 114:336, 1943.
4. Sorgo, W.: Ueber den Art. carotis interna, Verschluss bei jüngeren Personen, Ztschr. f. d. ges. Neurol. u. Psychiat. 167:581, 1939.
5. Gladston, M., Govons, S., Wortes, B. S., Steele, J. M., and Taylor, H. K.: Thrombosis of common, internal and external carotid artery, Arch. Int. Med. 67:1162, 1941.
6. Wolfe, H. R. I.: Unexplained thrombosis of the internal carotid artery, Lancet 2:567, 1948.
7. Ameli, N. O., and Ashby, D. W.: Non-traumatic thrombosis of the carotid artery, Lancet 2:1078, 1949.
8. Gurdjian, E. S., and Webster, J. E.: Thrombosis of internal carotid artery in the neck and in the cranial cavity: Symptoms and signs, diagnosis and treatment, Tr. Am. Neurol. A. 76:241, 1951.
9. Webster, J. E., Dolgoff, S., and Gurdjian, E. S.: Spontaneous thrombosis of the carotid arteries, Arch. Neurol. & Psychiat. 63:942, 1950.
10. Fisher, M.: Occlusion of the internal carotid artery, Arch. Neurol. & Psychiat. 65:346, 1951.
11. Johnson, H. C., and Walker, A. E.: The angiographic diagnosis of spontaneous thrombosis of the internal and common carotid arteries, J. Neurosurg. 8:631, 1951.
12. Elvidge, A. R., and Werner, A.: Hemiplegia and thrombosis of the internal carotid system, Arch. Neurol. & Psychiat. 66:752, 1951.
13. Chiari, H.: Ueber das Verhalten des Teilungswinkels der carotis communis bei der endarteriitis chronica deformans, Verhandl. d. deutsch. path. Gesellsch. 9:326, 1905.
14. Hunt, J. R.: The role of the carotid arteries, in the causation of vascular lesions of the brain, with remarks on certain special features of the symptomatology, Am. J. M. Sc. 147:704, 1914.
15. Hultquist, G. T.: Ueber Thrombose und Embolie der Arteria carotes und hierbei vorkommende Gehirnstörungen, Jena, Gustav Fischer, 1942.
16. King, A. B.: Massive cerebral infarction producing ventriculographic changes suggesting brain tumor, J. Neurosurg. 8:536, 1951.
17. Keele, C. A.: Pathological changes in the carotid sinus and their relation to hypertension, Quart. J. Med. N. S. 2:213, 1933.
18. King, A. B., and Langworthy, O. R.: Neurologic symptoms following extensive occlusion of the common or internal carotid artery, Arch. Neurol. & Psychiat. 46:835, 1941.
19. Noran, H. H., Baker, A. B., and Larson, W. P.: Central nervous system in pneumonia (nonsuppurative pneumonic encephalitis): III. An experimental study, Arch. Neurol. & Psychiat. 58:671, 1947.

Effects of Uremia on Cerebral Blood Flow and Metabolism

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SOME of the most common symptoms of uremia seem to have a neurologic basis, and pathologic studies of the central nervous system in young patients with uremia of extra-renal origin have shown widespread tissue changes involving both the nerve cells and the parenchymal elements.[1] Although it is not known to what extent the metabolic disturbances of uremia are responsible for neurologic symptoms, since uremia is also frequently accompanied by widespread vascular disease, there seems to be little doubt that many of the neurologic signs are based on a disturbance in function of cerebral cells related to uremia. These neurologic signs include striking alterations in mental status (varying from memory and personality disturbance to lethargy and coma) and convulsions. Even extensive motor signs such as hemiplegia have been ascribed to this syndrome.[2]

The present study was undertaken in an effort to measure the effects of severe uremia on cerebral circulation and metabolism, as measured by the nitrous oxide technic. Conclusions drawn from this study are necessarily limited by the absence of correlative observations on blood pH, carbon dioxide combining power, and specific electrolyte studies including blood potassium, calcium, and sodium. Sufficient information has emerged from these preliminary observations, however, to warrant reporting them now, particularly since the results differ somewhat from those reported by Heyman, Patterson, and Jones in 1951.[3]

METHOD

Seven subects with uremia were studied. Uremia was due to chronic glomerulonephritis in four patients, to pyelonephritis in one, and related to vascular disease in two. In all instances the clinical impression of uremia was

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This investigation was supported by a research grant (H-832) from the National Heart Institute of the National Institutes of Health, U. S. Public Health Service, and by a research grant from the National Multiple Sclerosis Society.

TABLE 1

EFFECTS OF UREMIA ON CEREBRAL CIRCULATORY AND METABOLIC FUNCTIONS

Patient's Age	Clinical data and mental status	Cerebral blood flow	Arterial O_2 content	Arterial-cerebral venous O_2 difference	Cerebral O_2 consumption	Arterial-cerebral venous glucose difference	Cerebral glucose consumption	Mean arterial pressure	Cerebral vascular resistance	Cerebral venous O_2 tension
		Ml./min./100 gm. brain	Volume per cent	Volume per cent	Ml. O_2/min./100 gm. brain	Mgm. per cent	Mgm. glucose/min./100 gm. brain	Mm. Hg	Mm. Hg Ml. blood/min./100 gm. brain	Mm. Hg.
58	Nephrosclerosis, NPN 126. Alert	96	9.8	2.7	2.6	4.4	4.2	95	0.99	38
49	Pyelonephritis, NPN 115. Slightly confused	100	7.8	3.5	3.5	4.1	4.1	135	1.35	27
22	Chronic glomerulonephritis, NPN 108. Alert	67	5.4	2.8	1.8	1.4	1.0	90	1.43	28
41	Hypertensive cardiovascular renal disease. No congestive failure. NPN 340. Confused	43	7.4	4.5	1.9	13.0	5.6	155	3.60	28
43	Chronic glomerulonephritis, NPN 210. Alert	44	13.9	7.3	3.2	10.8	4.7	84	1.91	26
29	Chronic glomerulonephritis, NPN 222. Semistuporous	91	6.0	3.0	2.7	2.0	1.8	107	1.18	28
34	Chronic glomerulonephritis, NPN 200. Semistuporous	76	9.1	3.5	2.7	4.3	3.3	156	2.05	30
	Mean	74	8.5	3.9	2.6	5.7	3.5	117	1.79	29
	Normal mean	62.9	19.1	6.3	3.9	9.9	6.2	90.4	1.47	32
	P value	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	> 0.1	> 0.1

confirmed by appropriate laboratory studies. The patients ranged in age from 22 to 58 years, with a mean age of 39 years; the 20 individuals used as control subjects had an average age of 38 years and all were in normal health. All studies were done in the fasting state, and cerebral blood flow was measured by a modification[4] of the original nitrous oxide technic.[5] Cerebral oxygen and glucose consumption and cerebral vascular resistance were calculated as described previously.[4] Blood oxygen content was measured by a spectrophotometric technic.[6] Blood samples for oxygen and glucose were drawn before and after each cerebral blood flow measurement and the average of the two values for arterial-cerebral venous oxygen difference was used as the final value in table 1. Blood glucose content was measured by Nelson's modification of the Somogyi technic.[7] With the arm held at heart level, arterial pressure was measured every two minutes during the procedure, using the auscultatory technic. Mean pressure was calculated from the formula, Mean pressure = Diastolic pressure + 1/3 pulse pressure. Cerebral venous oxygen tension was calculated from percentage cerebral venous oxygen saturation by means of an oxyhemoglobin dissociation curve drawn for pH 7.3. The blood nonprotein nitrogen was determined by the Koch-McMeekin technic.[8]

RESULTS

Results are recorded in detail in table 1. The mean arterial oxygen content in patients with uremia was 8.5 vol. per cent as compared to a normal value of 19.1 vol. per cent, or less than half the normal. Mean cerebral blood flow was 74 ml./min./100 gm. brain, significantly higher than the normal for this age group. Values for cerebral blood flow were quite variable and no specific reason for this variability can be recognized in this study. There was no statistical correlation between cerebral blood flow and degree of anemia, though it would seem that the great reduction in mean arterial oxygen-carrying capacity in these subjects is probably responsible for the increased cerebral blood flow. No correlation could be drawn between cerebral blood flow and degree of elevation of the nonprotein nitrogen, nor between cerebral blood flow and mental status. The mean value for arterial-cerebral venous oxygen difference was 3.9 vol. per cent as compared to the normal of 6.3 vol. per cent. Mean cerebral oxygen consumption was 2.6 ml. O_2/min./100 gm. brain, significantly less than the normal value of 3.9. Mean arterial-cerebral venous glucose difference was 5.7 mg. per cent as compared to the normal mean of 9.9, and mean cerebral glucose consumption (3.5 mg. glucose/min./100 gm. brain) was also significantly reduced from the normal mean of 6.2. The mean arterial pressure of 117 mm. Hg was considerably greater than the normal mean value of 90 mm. Hg, but the mean cerebral vascular resistance (1.79 mm. Hg/ml. blood/100 gm. brain/min.) was not significantly greater than the normal mean value of 1.47. Four of the seven subjects had lower than normal values for cerebral vascular resistance, but there was no adequate correlation between cerebral vascular resistance and degree of anemia, elevation of nonprotein nitrogen, or any other measured function.

DISCUSSION

These studies demonstrate that there is a consistent depression of cerebral oxygen and glucose consumption of variable degree in uremia, and that this reduction in cerebral metabolism is not due specifically to a decrease in the rate of cerebral circulation, since mean cerebral blood flow is greater than normal. The reduction in cerebral metabolism shows no statistical correlation to degree of anemia, cerebral vascular resistance, elevation of nonprotein nitrogen, or alteration in mental status. It should be emphasized, however, that all these subjects were severely anemic. The reduction in oxygen-carrying capacity of their arterial blood should have necessitated a striking increase in cerebral blood flow in order to compensate for the limited quantity of oxygen available to the brain cells for extraction from each unit of blood. It would appear that one of the limitations for the degree of oxygen extraction from capillary blood is the effective oxygen tension in the blood. In these subjects cerebral venous oxygen tension was not reduced significantly below normal. This may indicate that oxygen extraction from the blood by brain cells stops at approximately this level of oxygen tension, notwithstanding the total oxygen-carrying capacity of the blood; or it may indicate that cerebral tissue in uremia has suffered some type of metabolic depression, resulting in inability to extract sufficient oxygen to lower the cerebral venous oxygen tension further. This question cannot be answered until the effects of uncomplicated anemia upon cerebral circulation and metabolism are studied more completely than they have been until now.

It is of interest to note that, although the subjects reported in this study were considerably more anemic than those reported by Heyman, Patterson, and Jones,[3] both groups showed a reduction in cerebral oxygen consumption from normal of about the same magnitude. This might imply that the degree of reduction in oxygen-carrying capacity is not the most important factor in the depression of cerebral oxygen consumption which occurs in uremic subjects, but it does not obviate the conclusion that further work is needed to clarify this point. The available data seem to indicate that the inability of cerebral cells to utilize oxygen normally in uremia is probably due to a combination of several factors, including anemia and the extensive chemical disturbances which occur in uremia. Our studies corroborate their findings in pointing out the lack of correlation between measured cerebral metabolism and alteration in mental status. In this respect these studies differ from our previously reported observations in subjects with vascular disease of the brain[9] and with pernicious anemia.[10] In addition, their studies showed a mean cerebral blood flow slightly less than normal in uremia, whereas the cerebral blood flow in our group was greater than normal in five of the seven subjects. One of the two subjects whose cerebral blood flow was below normal was also the least anemic of the entire group studied. While no final explanation for the disparity in cerebral blood flow between our subjects and theirs can be given, it is likely that anemia is responsible for it. The frequent occurrence of renal

acidosis in the presence of severe uremia[11] must also be considered in the explanation for increased cerebral blood flow in five of these subjects, but since pH and arterial carbon dioxide content were not measured no further comment is warranted.

The reduction in cerebral glucose consumption is consistent with the reduction in cerebral oxygen consumption. No final explanation can be given for this finding on the basis of available data. Since the arterial glucose levels were within normal limits, there was adequate glucose available for the cerebral cells to utilize. Their failure to do so may indicate a depression of metabolism of these cells rendering them incapable of consuming glucose normally; or, since glucose is ordinarily utilized by brain cells in an aerobic oxidative process, the reduction in cerebral glucose consumption may simply reflect the altered cerebral oxygen consumption.

SUMMARY

1. Cerebral blood flow, oxygen and glucose consumption, vascular resistance, and cerebral venous oxygen tension were measured in seven patients with uremia and compared with 20 normal subjects in the same age group.

2. Cerebral blood flow was increased above the normal mean in five of seven patients, and it is postulated that this increase is probably due to the associated anemia. The consistent reduction in cerebral oxygen and glucose consumption is probably due to a combination of anemia and the extensive chemical disturbances which occur in uremia. Cerebral venous oxygen tension and cerebral vascular resistance were within normal limits.

3. There was no correlation between measured cerebral metabolism and nonprotein nitrogen level or mental status.

REFERENCES

1. Knutson, J., and Baker, A. B.: The central nervous system in uremia. A clinicopathologic study, Arch. Neurol. & Psychiat. 54:130, 1945.
2. Fishberg, A. M.: Hypertension and Nephritis, ed. 4, Philadelphia, Lea and Febiger, 1939.
3. Heyman, A., Patterson, J. L., Jr., and Jones, R. W.: Cerebral circulation and metabolism in uremia, Circulation 3:558, 1951.
4. Scheinberg, P., and Stead, E. A., Jr.: The cerebral blood flow in male subjects as measured by the nitrous oxide technique: Normal values for blood flow, oxygen utilization, glucose utilization, and peripheral resistance, with observations on the effect of tilting and anxiety, J. Clin. Investigation 28:1163, 1949.
5. Kety, S. S., and Schmidt, C. F.: The nitrous oxide method for the quantitative determination of cerebral blood flow in man: Theory, procedure, and normal values. J. Clin. Investigation 27:476, 1948.
6. Hickam, J. B., and Frayser, R.: A spectrophotometric determination of blood oxygen, J. Biol. Chem. 180:457, 1949.
7. Nelson, N.: A photometric adaptation of the Somogyi method for the determination of glucose, J. Biol. Chem. 153:375, 1944.
8. Koch, F. C., and McMeekin, T. L.: A new direct nesslerization micro-Kjeldahl method and a modification of the Nessler-Folin reagent for ammonia, J. Am. Chem. Soc. 46:2066, 1924.
9. Scheinberg, P.: Cerebral blood flow in vascular disease of the brain, with observations on the effects of stellate ganglion block, Am. J. Med. 8:139, 1950.
10. Scheinberg, P.: Cerebral blood flow and metabolism in pernicious anemia, Blood 6:213, 1951.
11. Bradley, S. E.: Biochemical abnormalities during renal insufficiency, New England J. Med. 235:755 and 791, 1946.

Digitalgia Paresthetica and Gonyalgia Paresthetica

Robert Wartenberg, M.D.

A PATHOGENIC AGENT which acts generally and has a specific affinity for the peripheral nervous system may affect most of the peripheral nerves or all of them. A bilateral, symmetrical polyneuritis or a sensory polyneuritis results. But it is a well established clinical fact that, through such a general action, a single nerve of the body may be affected exclusively. This produces an isolated mononeuritis or an isolated sensory mononeuritis.

The classical representative of such an isolated sensory mononeuritis is meralgia paresthetica. *Meros* is the Greek word for thigh. The whole term thus means pain and paresthesias in the area of the thigh. This clinical entity is also known as Roth's, Roth-Bernhardt's, or Bernhardt-Roth's disease. The Russian neurologist, Roth of Moscow, and the German neurologist, Bernhardt of Berlin, both described this syndrome independently and in the same year, 1905.

Meralgia paresthetica, a neuritis of the lateral cutaneous nerve of the thigh, leads to dysesthesias, hypesthesia, paresthesias, and occasionally to pain on the lateral aspect of the thigh, affecting the nerve unilaterally or bilaterally. A distinction is made here between dysesthesias and paresthesias. Dysesthesia is a more general term, and applies particularly to abnormal sensations felt spontaneously without external stimulation. Paresthesias are abnormal sensations which are felt on external stimulation.

Every textbook contains a description of meralgia paresthetica. Unfortunately, however, this condition is not sufficiently well known in general practice. It is often misdiagnosed, and patients are treated for rheumatism, arthritis, and so on. All types of sensory neuritis are somewhat neglected in textbooks and in the literature. Wilson[1] devotes but eight lines to the discussion of sensory neuritis. Since its clinical manifestations are mild and inconspicuous, it is neglected by both patient and physician. Sensory neuritis is essentially a harmless, self-limiting, benign affection. Symptoms may be very mild and intermittent or remittent. The patient seldom seeks medical advice, and the disease is often discovered by pure chance. What Freud,[2] who him-

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self suffered from meralgia paresthetica, said of the disease is characteristic: "For months I didn't feel it or think of it." It must be assumed that sensory neuritis is more common than seems apparent.

In the discussion of sensory neuritis one point, though obvious, may need emphasis. Any sensory nerve or the sensory portion of a mixed nerve can be affected in exactly the same way as the lateral cutaneous nerve of the thigh, resulting in a clinical picture which is analogous to that of meralgia paresthetica. Among others, the following nerves have been found to be affected singly: auriculotemporal nerve; dorsal cutaneous nerve of the forearm; cutaneous branches of the spinal nerves; deep peroneal nerve; superficial peroneal nerve; saphenous nerve; calcaneal branches of the tibial nerve; dorsal digital nerves of the foot.

Affections of these nerves often produce very puzzling clinical pictures, but they are harmless and do not cause much discomfort to the patient. Their differential diagnosis may be as difficult as it is important. Among all types of neuritis, that of the sensory portion of the trigeminal nerve and that of the superficial branch of the radial nerve are particularly noteworthy.

In sensory neuritis of the trigeminal nerve, which is always unilateral, only the superficial sensibility is affected. The clinical picture may lead to suspicion of a cerebellopontine angle tumor. Invariably this has been the first diagnosis in all cases observed. Sensory neuritis of the trigeminal nerve is, however, a benign, nonprogressive, transient affection of self-limiting course. The trigeminal nerve is affected exclusively.

Affection of the superficial branch of the radial nerve produces a clinical picture known as cheiralgia paresthetica.[3] This may be of traumatic origin produced, for instance, by pressure of a tight band of a wrist watch, but commonly the cause is unknown. A patch of hypesthesia is found on the inner side of the thumb. The affection may be mistakenly attributed to spondylarthritis or to compression of the brachial plexus. Whether traumatic or not, the affection is purely peripheral, benign, and nonprogressive.

The "nerve stretching test" is highly characteristic and diagnostically important for sensory neuritis of any type. If the test is positive, the patient experiences pain and dysesthesias when the affected nerve is stretched briskly. Of course, the test can be performed only when the nerve is so situated that it can be subjected to stretching. When the nerve is affected and the limb is at rest, spontaneous dysesthesias may be very mild and felt only occasionally. However, when the limb is brought suddenly and briskly into a position in which the affected nerve is stretched, the patient experiences painful sensations or even severe pain in the area of the affected nerve. As soon as the limb is brought back into a normal position of rest, these sensations subside quickly. In sensory neuritis, a positive nerve stretching reaction, that is pain on stretching, has been found so constantly and invariably that the following can be said without reservation: "Every diseased peripheral, mixed or especially sensory nerve reacts with pain to brisk, passive stretching. This is a constant, very early and very late sign of every sensory neuritis."[4] If the reaction to the

nerve stretching test is negative, it can be said with certainty that there has never been a neuritis or that it has healed leaving no residuum.

Of all the variously localized types of mononeuritis which have come under observation, two stand out as particularly interesting, especially with regard to differential diagnosis. These are digitalgia paresthetica and gonyalgia paresthetica. An example of each is described.

DIGITALGIA PARESTHETICA

A middle-aged man felt soreness of the skin on the ulnar side of the little finger of his right hand. Assuming that he might have cut himself or have been bitten by a mosquito, he inspected the spot repeatedly but the skin appeared normal. Two or three weeks later, he casually touched the affected skin area and noticed that the skin over the ground phalanx of his right little finger felt numb. Once, when reaching for an object placed high above his head, the patient brought his right hand into a position of radial abduction and immediately experienced sharp, stinging pain along the whole outside of his little finger. During the next few weeks numbness of the skin extended distally and became more intense. The sharp pain on radial abduction of the hand or little finger increased in intensity. This subsided somewhat after two or three months, and disappeared completely after about six months. Only the numbness remained. At rest the patient had no complaints except for occasional ill-defined feelings of soreness, ticklishness, or a sensation of crawling in the skin on the ulnar side of the little finger.

On examination a sensory defect was found as indicated in figure 1. The skin appeared normal, and pressure evoked no tenderness of the tissues or of the nerves in the affected area. On repeated examinations performed with various technics under different conditions, it was invariably found that radial abduction of the little finger or of the whole hand always produced painful sensations on the ulnar side of the little finger. The pain radiated "like electric shock" from the fifth metacarpophalangeal joint to the tip of the little finger. The more sudden and extensive the abduction, the more intense was the pain.

The area of sensory defect was exactly the same area as that supplied by the dorsal digital nerve. The dorsal digital nerve of the little finger is a terminal branch of the dorsal branch of the ulnar nerve to the hand. It was evident that, in all the maneuvers mentioned, stretching of the nerve produced pain.

There is no doubt that this patient had an isolated affection of the dorsal digital nerve of the little finger. A pair of such nerves run respectively on the external and internal borders of the dorsum of the little finger, and the external branch seems to have been affected in this case.

Traumatic affections of the digital nerves of the fingers have been described, but the author has observed only one such case. A girl crushed her left index finger in a lead-lined door and sustained a laceration on the palmar side of the finger at the distal interphalangeal joint. On examination six hours later, she complained of throbbing pain and numbness at the finger tip. There

FIG. 1. Digitalgia paresthetica. Isolated neuritis of the dorsal digital nerve of the little finger (N. dorsalis digiti quinti ulnaris). Dots indicate border of hypesthesia to touch; crosses indicate border of hypalgesia.

was hypesthesia extending over the radial half of the end phalanx of the index finger.

No published reference to nontraumatic neuritis of a digital nerve as described here has been found by the author.

GONYALGIA PARESTHETICA

A middle-aged man noted that during several weeks preceding examination he had attacks of painful sensation, each lasting a few seconds. This sensation was limited strictly to a small area of the skin below and lateral to the right knee. It occurred only when the patient pressed his flexed right knee against the mattress when getting into bed. The pain subsided immediately as soon as he stretched out his legs. He consulted his physician who could give no explanation for the pain. Since the patient continued to experience these episodes, he went to his physician who again was unable to explain the affection, but considered gout as a possibility. A few weeks later, the patient casually put his hand on his right knee and noticed a numb spot there. On a third examination, the physician found an area of hypesthesia the size of the palm of the hand, just below and lateral to the patella. All sensory modalities were involved.

A detailed examination one and a half years later revealed the sensory defect shown in figure 2. The patient had no definite symptoms on the corresponding area on the left side. However, he mentioned that occasionally there was "some ticklish feeling" on that side too. Both patient and doctor were surprised to find that there was a sensory defect on the left at a site which corresponded symmetrically to the defect on the right. However, the left-sided defect was less pronounced (figure 2).

This patient's condition has existed for about four or five years, but the actual time of onset is not definite. Throughout those years the patient has had practically no complaints in the affected area. Occasionally, however, he experiences "tingling," "pins and needles," or a "ticklish" sensation in the area. He has a painful sensation when he presses or knocks the bent knee against any object.

The site of dysesthesia occurring spontaneously and on bending the knee or on pressing it against an object, as well as the location and size of the defect in sensibility, leave no doubt that the infrapatellar branch of the saphenous nerve is affected. Extending downward along the medial aspect of the knee, the saphenous nerve pierces the deep fascia between the tendons of the sartorius and gracilis muscles. At this level the saphenous nerve gives off its infrapatellar branch. This curves forward and under the patella and the head of the tibia. With other branches of the femoral and the lateral external sural nerves, it forms the patellar nerve plexus.

At the author's request, Dr. J. B. deC. M. Saunders has made a special study of the infrapatellar branch of the saphenous nerve. His report follows:

"In the standard textbooks it is customarily stated that the infrapatellar branch of the saphenous nerve perforates the sartorius muscle and the fascia lata to spread out over the

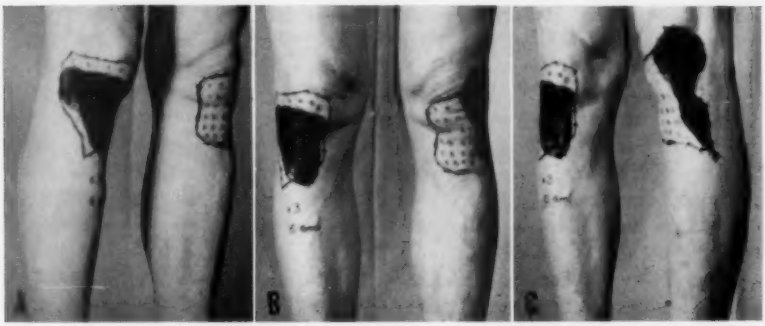

FIG. 2. Gonyalgia paresthetica. Neuritis of infrapatellar branch of saphenous nerve. Pain sensation tested with 6 gram algesiometer; touch sensation with No. 3 von Frey hair. Temperature (cold) sensation and perception of wetness tested with ether-moistened cotton. Dark area indicates complete loss of pain, touch, cold, and wet sensation. Stippled areas indicate complete loss of touch and temperature (cold sensation); preservation of wet sensation and diminution but not complete loss of pain sensation.

front of the knee where it forms, by uniting with the branches of the medial and intermediate (sometimes also lateral) cutaneous nerves of the thigh, a plexus named the patellar plexus. Occasionally an author will add that this nerve may derive from the nerve to the vastus lateralis in place of the saphenous, that it may not perforate the sartorius muscle, or that it may be reduced not infrequently to two small perforating branches.

"The infrapatellar branch of the saphenous nerve was traced out in 20 bilateral dissections and in ten unilateral instances, making a total of 50 individual specimens. The course of the nerve was found to be most variable from subject to subject and in the same subject. The infrapatellar nerve was found to be a branch of the saphenous nerve in every instance except two, where it was totally replaced by the anterior division of the medial cutaneous nerve of the thigh. In two cases, both unilateral, the nerve was represented by two branches. The nerve perforated the substance of the sartorius muscle in a little more than half (30 specimens), perforated the tendon of the muscle in a little less than a quarter (ten specimens), or passed under the anterior border of the muscle or tendon in a little less than one quarter (eight specimens). Where the nerve was represented by two filaments, in one case the upper filament perforated the middle of the width of the muscle and the lower slipped beneath its anterior border; in the second case the upper filament pierced the muscle and the lower, the tendon.

"The level at which the nerve emerges from beneath the sartorius muscle is quite variable, even on the left and right sides of the same subject. Consequently its more superficial course is correspondingly inconstant. In most instances (31 specimens) the nerve emerged through or beneath the muscle or tendon anywhere from a point two inches above to one inch below the level of the knee joint, and in the remainder (17 specimens) it appears from two to as high as six inches above the level of the joint.

"Owing to the variability in level of emergence, the course of the nerve to the infrapatellar region varies from one which runs almost vertically for some distance, to another which is horizontal, and still another which passes obliquely downward.

"It is evident from inspection of a number of examples that the nerve is vulnerable at two points. The first is in the case where the nerve passes through a foramen in the tendon of the sartorius rather than through its muscular belly. The continual displacement of the tendon in flexion and extension may subject the nerve to the trauma of friction at its site of emergence. The second case is where the nerve emerges at a point just above

the knee joint so as to course almost horizontally across the medial femoral condyle at or just below its epicondyle. Here the nerve may be compressed against the bone where the knees are in contact."

The infrapatellar branch of the saphenous nerve is important orthopedically. Formerly it was sometimes unavoidably severed in operation for removal of the internal meniscus. Painful neurofibromata often resulted. Now, however, the incision is made above this branch in order to avoid such damage. Smillie[5] showed the area of anesthesia in one case where the nerve was divided by an incision to excise the medial meniscus. The area was similar to that shown in figure 2.

The superficial location of the infrapatellar branch of the saphenous nerve predisposes it to manifold injuries. Affection of the branch "is a fairly common injury in athletes and in its diagnosis most commonly missed, and needless surgery done to the knee cartilages in an attempt to relieve the patient of symptoms."[6] The literature contains comparatively little on traumatic injury to the infrapatellar branch, and traumatic neuritis is not even mentioned in many a comprehensive report on non-bony injuries to the knee. This seems to support the view expressed by Hitchcock.[6] What Gordon[7] described as "traumatic prepatellar neuralgia" is nothing else than a traumatic neuritis of the infrapatellar branch of the saphenous nerve. Gordon's cases show "1) a history of well-remembered violence to the front of the patella, usually in a fall; 2) after the injury, sometimes transient prepatellar swelling, not circumscribed by the bursa; 3) immediately or several weeks after the accident the onset of neuralgic pain deep to the patella, described usually as a dull ache 'like toothache' . . . ".

However, in the case described here trauma of any kind, chronic, acute, surgical, or orthopedic, can be excluded with certainty. Moreover, the bilaterality of the affection is against traumatic origin. Therefore, it must be assumed that here we are dealing with an intrinsic lesion of the nerve, with a non-traumatic neuritis.

Apparently such a neuritis has never been outlined as a clinical entity. Bing, to whom the author reported this observation briefly, wrote that he had never seen such a syndrome of bilateral neuritis of the infrapatellar branch of the saphenous nerve, nor had he ever read or heard of it. He regarded this case as an *"observatio princeps."*

The condition is not mentioned in the comprehensive works of Hohmann,[8] Cave,[9] Lewin,[10] Sonnenschein,[11] de Palma,[12] or Hackenbroch.[13] However, it probably has been observed and described somewhere, and the description buried in the vast literature. It may never have been recognized as neuritis, and its identity lost in the general discussion of pain in the knee. In the orthopedic literature it is not uncommon to find reports of pain at the knee where the knee joint is completely normal, clinically and roentgenologically. It is reasonable to assume that at least some of the cases are unrecognized cases of neuritis of the infrapatellar branch of the saphenous nerve.

The closest description of this clinical entity is given by Smillie[6] under

the heading, "Neuritis of a Branch of Patellar Plexus." He describes a condition "characterized by the complaint of an 'electric shock' when a small well-defined area of skin overlying the patella or the immediately adjacent regions, is subjected to the lightest touch . . . The etiology is obscure. It is merely assumed to be due to a minor direct injury which produces an irritative lesion of a minute sensory nerve. On examination the 'trigger area' can usually be found, adjacent to which is a small area of hyperaesthesia in the region of the patellar plexus." The patient "may be reassured that although the condition may remain for a few weeks, it is self-limiting and will disappear as suddenly as it came."

In a private communication Smillie reports that he himself has suffered from this condition. The sensitive area of the skin caused him "quite a disability from the electric shock produced from the clothing coming in contact with the skin." Though the symptoms may be alarming, the condition "is self-limiting, and disappears with patience and without treatment." It is almost always misdiagnosed.

The "electric shock" described by Smillie is probably due to traumatization of the diseased nerve by stretching and pressing when the knee is bent. The clinical manifestations in the case described here are milder than those described by Smillie. but it is well known that neuritis varies markedly from person to person. Hyperesthesia was not present in the case described here. Smillie merely assumed the condition to be traumatic, but had no evidence to support this view. The duration of the author's case may be reckoned in years, and not in weeks as in Smillie's cases. Despite these differences it must be assumed that what he described was a case of nontraumatic neuritis of the infrapatellar branch of the saphenous nerve.

The peculiar case described by Mellinkoff and Mellinkoff[14] was probably one of a traumatic neuritis of this nerve. Here, in an eight month old infant, an "area of the skin about two and one-half inches (6.4 cm.) in diameter around the left tibial tubercle became covered with beads of moisture." This localized hyperhidrosis occurred only while the baby was nursing and slowly disappeared afterward. The authors assumed that crawling traumatized the superficial nerves over the left knee. This caused the cholinergic nerve to become hypersensitive, and sweating occurred when acetylcholine was disseminated by the blood stream following vagus stimulation. The "superficial nerves" mentioned were probably the infrapatellar branch of the saphenous nerve.

DISCUSSION

The most outstanding features of digitalgia paresthetica and gonyalgia paresthetica are the following: 1) insidious beginning; 2) long course, extending over years; 3) mildness of symptoms; 4) pain on nerve stretching; 5) absence of any complications, particularly on the part of the skin; and 6) absence of any indication in the history that the condition might have been caused by trauma, acute or chronic.

Since, etiologically, trauma does not appear to be the primary cause, the affection must be either metabolic or infectious in origin. Despite long observation and intensive investigation, no metabolic disturbance has ever been discovered by the usual laboratory and clinical methods. Though a metabolic disturbance still cannot be completely excluded, a toxi-infectious process of low virulence, particularly a virus infection, seems more probable. Some neurotropic viruses have a special affinity for the peripheral nervous system, or even for the sensory nerves only. Thus, a single sensory nerve alone may be affected. General constitutional symptoms and signs like fever, malaise, and so on may be absent. The process may be chronic.

Both in digitalgia paresthetica and gonyalgia paresthetica, the case history shows that at some time or other the patient has had a transient neuritis involving some other sensory nerve. This indicates that the cases of sensory mononeuritis described here are only a part of some general affection which existed over a period of years and isolatedly involved various sensory nerves.

But if a toxi-infectious process is acting generally, what predisposes a single nerve to the affection? The answer is its unfavorable location. When a pathogenic agent is acting on the peripheral nerves in general, those nerves which are normally subject to pressure and tension are first, most, or only affected. It may be that unfavorable location interferes with the blood supply to the nerve, and the consequent stagnation of the blood allows this nerve to be a *locus minoris resistentiae* for the toxi-infectious process. The digital nerves and the infrapatellar branch of the saphenous nerve, located very superficially, close to the bone, and running across joints that are much in use, certainly fall into the category of unfavorably located sensory nerves. The same is true for the lateral cutaneous nerve of the thigh, the affection of which produces meralgia paresthetica. It is a well established fact that this nerve, lying as it does under the tough Poupart's ligament, and often penetrating the sartorius muscle as well as the sturdy fascia of the thigh, is subject to pressure at several points.

Though both digitalgia and gonyalgia paresthetica are simple and insignificant clinically, they belong etiologically to the most obscure and puzzling affections of the nervous system. They raise many questions, to some of which the answer at present is unknown.

From a practical standpoint, the most important aspect of these two conditions is their differential diagnosis. This applies particularly to gonyalgia paresthetica. It must be recognized as such and not mistaken for an affection of the knee which may lead to needless surgical and orthopedic treatment.

Since the cause of these two types of neuritis is not known, there can be no causative treatment. Furthermore, the symptoms are usually so mild that no treatment is required.

SUMMARY

Just as an isolated neuritis of the lateral cutaneous nerve of the thigh leads to meralgia paresthetica, an isolated neuritis of the dorsal digital nerve of

the finger produces digitalgia paresthetica, and an isolated neuritis of the infrapatellar branch of the saphenous nerve produces gonyalgia paresthetica. Apparently such a neuritis is not due primarily to any local disturbance but to a general affection. This may be either metabolic or infectious, probably the latter. Any general infection with specific affinity for the peripheral nerves involves first and more readily those nerves which are, from an orthopedic standpoint, unfavorably located.

REFERENCES

1. Wilson, S. A. K.: Neurology, London, E. Arnold & Co., 1940, vol. 1, p. 307.
2. Freud, S.: Ueber die Bernhardt'sche Sensibilitätsstörung, Neurol. Centralbl. 14:491, 1895.
3. Wartenberg, R.: Cheiralgia paraesthetica, Ztschr. f. d. ges. Neurol. u. Psychiat. 141:145, 1932.
4. Wartenberg, R.: Stretching test in neuritis, California & West. Med. 55:76, 1941.
5. Smillie, I. S.: Injuries of the Knee Joint, ed. 2, Baltimore, Williams & Wilkins Co., 1951.
6. Hitchcock, H. H.: Personal communication.
7. Gordon, C. G.: Traumatic prepatellar neuralgia, J. Bone & Joint Surg. 34B:41, 1952.
8. Hohmann, G.: Leitsymptom: Knieschmerz, München. med. Wchnschr. 93:881, 1951.
9. Cave, E. F.: Nonbony injuries to the knee, S. Clin. North America 31:1355, 1951.
10. Lewin, P.: The Knee, Philadelphia, Lea & Febiger, 1952.
11. Sonnenschein, A.: Biologie, Pathologie und Therapie der Gelenke dargestellt am Kniegelenk, Basel, Benno Schwabe & Co., 1952.
12. de Palma, A. F.: Diseases of the Knee, Philadelphia, Lippincott, 1953.
13. Hackenbroch, M.: Der Knieschmerz, Deutsche med. Wchnschr. 78:357, 1953.
14. Mellinkoff, S. M., and Mellinkoff, J.: Gustatory hyperhidrosis of the left knee, J.A.M.A. 142:901, 1950.

Considerable interest attaches to the march of fits which begin locally, and of which the case just mentioned is an example. It is scarcely possible to consider this subject without referring it to certain pathological questions which are involved, and which would find a more logical, although less convenient, place in the chapter on Pathology. In that place the theory here assumed, that the discharge in epilepsy originates in the cerebral hemispheres, will be further discussed.

Hughlings Jackson has drawn attention to the frequency with which the fits begin in the hand, and associated with it the law that the spasm most frequently begins in small muscles which are put to the most varied uses, and he has put forward also the hypothesis that these small muscles are represented by small cells, and that such cells are less "stable" than larger ones. But it is important to note that (as stated in the description of modes of onset) a large number of fits beginning in the hand commence, not by a motion, but by a sensation. No doubt in these the same general principle holds good: the sensory centres in which the hand is represented are much more highly developed than those in which the upper part of the arm is represented. But the law holds good only generally, not universally, with regard to either motor or sensory aurae. The thumb and forefinger are the parts put to the most varied uses, but initial spasm, though it sometimes occurs in them, occurs more frequently in some other part of the hand, and an initial sensation is much less frequently felt in the parts of the hand in which sensation is most highly developed – the palmar aspect of the fingers – than in some other part, as the knuckles or the wrist.

W. R. Gowers in *Epilepsy and Other Chronic Convulsive Diseases*, published in 1885.

Mebaral as an Anticonvulsant

Harold Berris, M.D.

MEPHOBARBITAL (Mebaral) is an effective anticonvulsant which has the further attribute of low toxicity. Indeed, the occasional toxic reaction that does occur with Mebaral is rapidly reversible and of no serious consequence. This drug has not received adequate recognition as an anticonvulsant. Because of the paucity of literature on its use for control of seizures, it is felt that it would be of value to present experiences with this drug in a relatively large group of patients, the majority of whom have been followed for several years. The patients studied were all followed in the seizure clinic of the University of Minnesota Hospitals.

Mebaral was first introduced in Europe in 1929 under the name, Prominal. This drug is the 3-methyl derivative of phenobarbital and bears the relation to it which Mesantoin does to Dilantin; however, Mebaral is less toxic than phenobarbital, in contradistinction to the comparative toxicity of Mesantoin and Dilantin.[1,2]

In 1932 Blum[3] reported on the results of Mebaral therapy in several hundred seizure patients after three years of treatment. He found that doses of 0.2 gm. (3 grains) given two to three times daily decreased seizures by 50 per cent. Its value as an anticonvulsant in patients with petit mal seizures was also reported by Blum. Gibbs,[4] too, found it an effective agent for petit mal (pyknolepsy and myoclonic seizures). He pointed out that it is of particular value when used with Tridione, since it reduces the likelihood of grand mal seizures which may occur when that drug is used alone. Heyde[5] found Mebaral slightly superior to phenobarbital as an anticonvulsant, but felt that it was much more potent in alleviating the psychic symptoms in epilepsy. This is in accord with the work of Page.[6] Meller and Resch,[7] in a study involving 255 patients on most of the standard anticonvulsants, reported that Mebaral and phenobarbital were comparable in efficacy but the incidence of toxicity with phenobarbital was approximately three times that of Mebaral.

CLINICAL STUDY

Three hundred and sixty-three patients have been studied in the seizure clinic at this hospital; 170 were females and 193, males. The patients ranged in age from 16 to 70, with an average age of 33.4 years. All types of seizures

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These studies aided by a grant from the Teagle Foundation.

were represented in this group – grand mal, petit mal, minor, psychomotor, diencephalic, and focal seizures of all varieties. Etiologically, trauma, infections, tumor, toxins, metabolic and vascular diseases were represented, but in many cases the etiology was not determined. The investigation of each patient included skull roentgenogram, electroencephalogram, serum calcium and phosphorus, and fasting blood sugar. Pneumoencephalograms were done in almost half of the patients.

Over 90 per cent of the patients (320) had been on Mebaral alone or Mebaral in combination with other anticonvulsants. When Mebaral alone was used, the average dose was 0.1 gm. (1½ grains) three times a day, but as much as 0.2 gm. three times daily was given; the minimal dosage was 0.1 gm. daily.

EVALUATION OF DRUG THERAPY

In the entire group of patients, 75 had a follow-up period of six months or less. These will be treated separately since the results would be considered inconclusive. However, in view of the findings in the remaining 288 patients, it would appear that the action of the drug is fairly consistent. The results are classified in the following manner:

Excellent control = 1 seizure in 8 to 12 months.
Good control = 1 seizure in 3 to 8 months.
Fair control = 1 seizure in 1 to 3 months.
Poor control = several seizures a month.

Of the 75 patients treated for six months or less, Mebaral was given in 56 cases. It provided excellent or good seizure control, either alone or in combination with other anticonvulsants, in 18 of 25 patients in whom follow-ups were possible. In a few instances it was found that Mebaral was superior to phenobarbital. No serious toxic effects were seen. Since these cases were not followed for an adequate period, further breakdown of this group does not seem indicated.

Of the 288 patients followed for more than six months, 36 patients were maintained on Mebaral alone, and of these 17 showed excellent control and 13 good control (a total of 82 per cent). Mebaral was effective in all types of seizures. When used alone it produced excellent or good control in 19 of 21 patients with grand mal seizures. Of the remaining 15 patients, in whom all the other seizure patterns and mixed seizure patterns were represented, 11 showed excellent or good control.

One hundred and seven patients were given Mebaral and Dilantin. In 67 of these the two drugs were started simultaneously, and 26 showed excellent control, 21 good control, 12 fair control, and seven poor control (70 per cent excellent or good control). The discrepancy between the results obtained with Mebaral alone (82 per cent) and that obtained with Mebaral and Dilantin (70 per cent) is probably due to the fact that the disorder was more severe in patients treated with the combined drugs, while milder cases were treated with Mebaral alone. In 40 patients either Mebaral or Dilantin was given initially and the other drug added at a later date. In 14 patients who

TABLE 1
INCIDENCE OF TOXICITY FROM MEBARAL AND OTHER ANTICONVULSANTS

Drug	*Number of patients*	*Gum hypertrophy*	*Ataxia*	*Drowsiness*	*Nausea, vomiting*	*Rash*	*Visual disturbances*	*Blood dyscrasia*	*Liver damage*	*Psychosis*	*Total toxicities percentage*
Mebaral	320	..	1	9	2	3	..	..	..	..	4.7
Dilantin	232	14	24	..	..	6	1	..	..	..	13.4
Phenobarbital	116	..	..	21	..	4	..	..	..	..	22.3
Phenurone	22	..	..	..	..	2	..	..	3	2	36.3
Mesantoin	49	..	2	..	1	5	3	3	..	..	28.6
Tridione	24	..	..	..	..	1	7	..	..	..	33.3
Paradione	8	..	..	..	..	..	..	..	..	..	...
Thiantoin	16	..	..	..	1	..	..	..	..	..	...

were first placed on Dilantin, there was definite improvement in seizure control after the addition of Mebaral. In a comparable group who were first placed on Mebaral, only four improved after addition of Dilantin.

Fifty-eight of 107 patients treated with Mebaral and Dilantin had grand mal seizures, and 43 had an excellent or good response. The remaining 49 patients had mixed seizure patterns and 34 showed excellent or good control, thus suggesting that the addition of Mebaral may supplement the action of Dilantin in the control of all types of seizure disturbances.

Perhaps even more impressive than its seizure control is the lack of toxicity from Mebaral when compared to other anticonvulsants in general use. All of the standard anticonvulsants were used in the clinic and the incidence of toxicity associated with the use of many of these drugs is compared with that of Mebaral in table 1.

The incidence of toxicity of Mebaral in 320 patients was 15 (4.7 per cent), which is considerably less than that found with the other safe anticonvulsants such as phenobarbital and Dilantin. In no case was the toxic effect irreversible, nor did any toxic reaction constitute a threat to life. All patients who complained of excessive drowsiness with Mebaral were receiving 0.2 gm. three times a day, and the symptoms disappeared promptly on reducing the drug.

DISCUSSION

Experience has indicated that Mebaral is superior to phenobarbital as an anticonvulsant of the barbiturate series, and as a result is now the barbiturate of choice in the treatment of convulsive disorders in the seizure clinic at the University of Minnesota Hospitals.

Most references in the literature state that Mebaral may be used in place of phenobarbital in a dosage twice that of phenobarbital and that the results are comparable.[8,9] The above conclusions show that results are similar with respect to anticonvulsant activity, but the extremely low incidence of toxicity

with Mebaral is of utmost importance to the patient. It affords more efficient function and less loss of time from normal activity for treatment of the toxic reaction.[2,7,10,11] Mebaral, therefore, is an excellent drug in the treatment of mild convulsive disorders, particularly since it so rarely adds to the patient's incapacity.

Not only is the drug an effective agent when used alone, but it greatly enhances the improvement obtained when added to Dilantin therapy, at the same time obviating the risk of toxicity where the dosage must be increased progressively to obtain the desired response.

This drug is effective in treating all types of convulsive disorders. It is a particularly useful adjunct to Tridione and Paradione therapy in petit mal seizures, since it serves to enhance the response of either Tridione or Paradione due to its effective action against petit mal spells, while also reducing any possible exacerbation of grand mal seizures. The addition of Mebaral to Tridione or Paradione also enables one to reduce the dose of the latter drugs and thus reduce the danger of the toxic action of these drugs.

SUMMARY

1. The use of Mebaral as an anticonvulsant is reviewed.

2. The effective anticonvulsant dose when used alone is between 0.1 and 0.2 gm. (1.5 to 3 grains) three times a day.

3. The drug is effective against all types of seizures.

4. Its anticonvulsant activity compares favorably with phenobarbital and in some selected cases is superior to it.

5. When it is used in conjunction with other anticonvulsants, better seizure control is usually obtained.

6. The addition of this drug to other anticonvulsants often makes it possible to reduce dosage of the latter, thereby reducing danger of toxicity. toxicity.

7. Mebaral is the least toxic of all the standard anticonvulsant medications, and its toxic reactions are never of a serious nature.

Mebaral is a product of Winthrop-Stearns, Inc.

REFERENCES

1. Weese, H.: Zur Pharmacolie des Prominal, Deutsche med. Wchnschr. 58:696, 1932.
2. Abbott, J. A., and Schwab, R. S.: The serious side effects of the newer anti-epileptic drugs, New England J. Med. 242:943, 1950.
3. Blum, E.: Die Bekämpfung epileptischer Anfälle und ihrer Folgeerscheinungen mit Prominal, Deutsche med. Wchnschr. 58:696, 1932.
4. Gibbs, F. A.: New drugs of value in the treatment of epilepsy, Ann. Int. Med. 27:548, 1947.
5. Heyde, H.: Ueber Prominal und Luminal-Wirkung bei schweren epileptischen Erkrankungen, Klin. Wchnschr. 11:1874, 1932.
6. Page, L. G. M.: Prominal in epilepsy, Brit. M. J. 1:531, 1936.
7. Meller, R. L., and Resch, J. A.: Convulsive disorders in adults, Postgrad. Med. 6:452, 1949.
8. Carter, S.: Convulsive disorders, M. Clin. North America 37:315, 1953.
9. Ives, E. R.: Comparison of various drugs in treatment of epilepsy, J.A.M.A. 147:1332, 1951.
10. Kaufman, C., and Isenberg, S.: Antiepileptic drugs, M. Clin. North America 36:1381, 1952.
11. Cohen, B., and Myerson, A.: Mebaral in the treatment of epilepsy, New England J. Med. 227:336, 1942.

Motor Deficits Produced by Posterior Rhizotomy Versus Section of the Dorsal Funiculus

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THE POSSIBLE ROLE of the afferent system in initiating, directing, and controlling voluntary movements has not been fully ascertained. The key to unlocking the mysteries of this important function may lie in the direction of its afferent connections and influences. Gooddy[1] states that sensation and motion cannot be divided anatomically nor physiologically and that the two actually form a single, continuous process. He believes that the motor cortex is conditioned ontogenetically from the first to perform movements by receptors. Quantitatively, it is known that the somatic afferent division surpasses the efferent. It has many more fibers coursing into the primate, central nervous system; there are more sensory tracts in the brain and spinal cord and its central cellular connections including the thalamus and sensory cortex requires billions of nerve cells.

One of the methods utilized to study the afferent aspect of motion is that of producing lesions in various parts of the system and then noting the physiologic deficits produced. Investigations of this nature in monkeys have been made on divisions which can be approached surgically; on the dorsal roots;[2–5] on the posterior columns;[6] and on the parietal cortex.[7,8] Combined lesions, involving more than one portion of the afferent system, apparently have not been performed nor have the effects of one operation been compared critically with those of another.

On the basis of known physiologic facts, it might be assumed that any motor deficits resulting from lesions made either in the dorsal roots of peripheral nerves, in the dorsal columns of the spinal cord, or in the parietal cortex of the cerebrum are due to loss of afferents arising from the muscles, tendons, and joints. If this is true, then the symptomatology should be somewhat identical irrespective of which one of the three is ablated. Having found that a very severe and enduring type of paralysis follows section of all the dorsal roots to an upper extremity,[4,5] it was felt that it might be of value to compare this finding with that obtained in chronic animals following high section of

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This investigation was supported by a research grant from the National Institutes of Health, U. S. Public Health Service.

the posterior columns. This part of the spinal cord represents dorsal root neurons of the first order which serve to carry proprioceptive impulses to such higher centers as the sensory cortex and possibly the cerebellum.

MATERIAL AND METHODS

Section of the posterior columns bilaterally at the level of the first cervical segment, in which the accuracy of placements was judged to be relatively unequivocal, was performed in eight monkeys. These were selected from a larger group operated upon. A sharp knife with a curved blade was utilized in making the lesions. The experimental animals were allowed to survive postoperatively for an average of two months, during which time they were studied and compared physiologically with the dorsal root series as to motor function. By comparison, Ferraro and Barrera[6] in their investigation, sectioned the posterior columns in monkeys at the level of cervical four or five and lower levels and sacrificed them on the twelfth day postoperatively. Following autopsy, histologic studies through, above, and below the level of the lesions were made to determine the degree of involvement of the proprioceptive tract.

RESULTS

There is a wide difference in the motor behavior of monkeys following section of the dorsal roots on the one hand and the dorsal columns on the other.

When all the dorsal roots to an upper extremity are cut in the adult monkey, severe and enduring deficits characterized by an almost complete loss of purposeful movements occur immediately. Flaccidity is an outstanding feature and many reflexes including the postural are affected. Quoting from a previous investigation,[4,5] "impulses, coursing over this system, seem to have a priming effect on motor cells within the central nervous system, without which initiation and direction of motor phenomena is impossible." Such animals are unable to use the involved extremity for eating or other vital purposes. The phenomenon of restitution of function did not occur. It was felt that this portion of the afferent system might be very important in training upper and lower motor neurons to function normally and in the restitution of function and production of spasticity following lesions in the brain and spinal cord.

By contrast, the motor deficits following section of the dorsal columns at the level of cervical one are much more minimal in respect to effect on posture, tone, and movement. No true paralysis occurs. The ability to use the appendages for postural support remains, the tone in the muscles is much greater, and movements involving sitting, standing, walking, running, and eating can be affected without too much difficulty. Initially there is loss or diminution of position sense, spontaneous grasping, and hopping and placing reactions. The deep reflexes tend to be increased. A small and varying amount of hypotonia is present which does not come close to matching that occurring

in dorsal rhizotomy. These findings agree with the acute study of Ferraro and Barrera[6] on posterior column section in the monkey. However, all of these defects appear to be temporary as restitution of function, which fails to develop in dorsal root section of adult animals, is judged to be complete or nearly complete two months postoperatively.

COMMENTS

Experimental studies on the comparison of motor deficits following dorsal root versus posterior column section should be of interest because the results may present clues as to the etiology of symptoms in tabes dorsalis in man. This disease is a process which essentially attacks the posterior roots in syphilis, most often in the lumbar region, and produces a definite class of motor symptoms characterized by inability to regulate the direction, rate, force, and extent of voluntary movements. The defects may lead to complete paralysis atlhough motor power in the limbs may remain unimpaired.[1] The cause of such deficits is attributed to involvement and loss of the afferent component arising within the spindles of striated muscle. The results of the present investigation suggest that other neurons within the posterior roots than those which ascend in the posterior columns may be of importance in the over-all function of motor physiology, at least in the monkey.

There are several features in an analysis of the general problem which seem to be pertinent. One is that, no matter how much degeneration there might be in the posterior roots, the only tangible evidence of it from examination of the spinal cord will be seen in the posterior columns. This is because the fasciculus gracilis and cuneatus consist of fibers from the roots which ascend without synaptic interruption. Most of the nonmuscular afferents (cutaneous and visceral) of the dorsal root system terminate, as far as we know, in the region of the posterior gray matter. From here secondary neurons arise which course to higher centers. A second point is that involvement of other afferents within the posterior root system than that of the muscular group may account for some of the symptomatology. Thirdly, it is also possible that muscular afferents may course upward in the spinal cord in localized regions outside of the posterior columns.

The fact that the posterior column alone shows ascending degeneration following pathology in the dorsal roots can be misleading because it suggests that its involvement accounts for all the symptomatology. It is known that the pathologic process in tabes dorsalis can affect more than just the muscular afferent neurons. When this occurs, it is possible that such fiber divisions as touch, pressure, pain, temperature, and even the visceral sensory may affect the priming or functioning of motor cells within the central nervous system.

In respect to the possibility of sensory modalities other than muscle afferents being important in motor function, Denny-Brown[9] rates touch of high rank. He regards the motor cortex as functioning essentially as a tactile mechanism, and considers that it is a facilitating mechanism acting on the segmental proprioceptive setup below and controlled in great part by tactile

stimulation. To him, area 4 is the chief center of the "sensorimotor cortex" of J. Hughlings Jackson.

Results of a recent investigation by Gardner and Haddad[10] support the view that muscular afferents, possibly the majority, may course rostrally in the spinal cord outside of the posterior columns. They found that impulses initiated by electrical stimulation of afferents, arising from muscles and joints in the lower extremity of the cat, may reach the cerebral cortex by traveling in the anterolateral part of the spinal cord. Section of the dorsal funiculi did not abolish the evoked potentials they produced.

On the basis of the diverse results obtained in the monkey, following dorsal rhizotomy on the one hand and section of the posterior columns on the other, as well as consideration of other recent findings,[9,10] it seems permissible to assume that the classical description given for function of the posterior columns in motor function may be questioned.

CONCLUSIONS

Motor deficits resulting from lesions destroying all posterior column fibers at the level of cervical one in the monkey are minor and temporary compared with those following complete dorsal rhizotomy. No true paralysis occurs in the former and the appendages can be used for postural support, sitting, standing, walking, running, and eating. The initial abnormal symptoms consisting of diminution in both position sense and spontaneous grasping and slight hypotonia return gradually to normal or near normal by the end of two months postoperatively. It is assumed that other posterior root fibers than those which course upward in the posterior columns in the monkey contribute to motor physiology. Either the cutaneous or visceral afferents are of importance or muscle afferents ascend in other parts of the cord.

REFERENCES

1. Goodby, W.: Sensation and volition, Brain 72:312, 1949.
2. Sherrington, C. S., and Mott, F. W.: Experiments upon the influence of sensory nerves upon movement and nutrition of the limbs, Proc. Roy. Soc. 57:481, 1895.
3. Kopczynski, S.: Recherches experimentales, physiologiques et anatomiques sur les racines posterieures des nerfs spinaux, Poln. Arch. med. Wiss. 3:99, 1907.
4. Lassek, A. M.: Inactivation of voluntary motor function following rhizotomy, J. Neuropath. & Exper. Neurol. 12:83, 1953.
5. Lassek, A. M.: Potency of isolated brachial dorsal roots in controlling muscular physiology, Neurology 3:53, 1953.
6. Ferraro, A., and Barrera, S. E.: Summary of clinical and anatomical findings following lesions in the dorsal column system of macacus rhesus monkeys, A. Res. Nerv. & Ment. Dis., Proc. 15:371, 1935.
7. Kennard, M. A., and Kessler, M. M.: Studies of motor performance after parietal ablations in monkeys, J. Neurophysiol. 3:248, 1940.
8. Peele, T. L.: Acute and chronic parietal lobe ablations in monkey, J. Neurophysiol. 7:269, 1944.
9. Denny-Brown, D.: Disintegration of motor function resulting from cerebral lesion, J. Nerv. & Ment. Dis. 112:1, 1950.
10. Gardner, E., and Haddad, B.: Pathways to the cerebral cortex for afferent fibers from the hindleg of the cat, Am. J. Physiol. 72:475, 1953.

Arteriovenous Malformations of the Great Vein of Galen

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ARTERIOVENOUS malformations are usually situated along the surface of the brain and, as a consequence, they produce a symptomatology characterized chiefly by convulsions or intracranial hemorrhage. When these lesions occur away from the cortical surface, they produce different clinical manifestations. Russell and Nevin[1] first described this lesion involving the great vein of Galen, and subsequent publications[2–8] have increased the reported cases to ten. This paper is concerned with an additional case and an analysis of the symptomatology produced by arteriovenous malformations of the great vein of Galen.

CASE REPORT

A 52 year old man sustained a head injury in an automobile accident in 1941. He had complained of occasional headaches and episodes of dizziness for several years prior to hospitalization. On September 17, 1951, he arose complaining of a severe headache, suddenly lost consciousness, fell to the floor, and vomited. Shortly thereafter he was admitted to the hospital in a comatose state. The blood pressure was 145/70 and the body temperature was markedly elevated. There was a left hemiparesis and the left plantar response was extensor. Lumbar punctures on September 20 and 22 revealed grossly hemorrhagic cerebrospinal fluid. Routine urinalysis and hematologic and serologic studies were within normal limits. An electroencephalogram on September 21 revealed high voltage 1½ to 2½ per second activity over the entire right cerebral hemisphere, as well as spike activity over the right frontal and central region.

During hospitalization consciousness returned for brief periods, but restlessness and drowsiness persisted. On the tenth day following admission the patient suddenly expired.

Postmortem examination showed subarachnoid blood over the base of the brain, with some extension into the sylvian fissures and over the vertex. A tangled mass of vessels occupied the area of the great vein of Galen, encroached upon the parenchyma of the adjacent occipital lobes, and communicated bilaterally with the branches of the posterior cerebral arteries. A thin-walled vessel 0.8 cm. in diameter originated in the vascular mass and extended anteriorly in the cisterna ambiens, lying adjacent to the right cerebral ped-

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Read before the Scandinavian Neurologic Congress, September 12, 1952.

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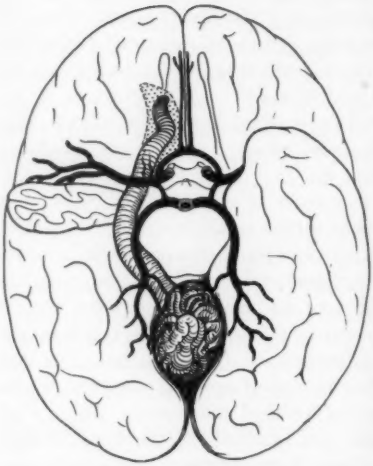

FIG. 1. Arteriovenous malformation in the region of the great vein of Galen. A thin-walled vessel originating in the malformation extends anteriorly on the inferior surface of the cerebral hemisphere to enter the frontal horn of the lateral ventricle.

FIG. 2. Vascular malformation exhibiting arterial and venous elements with interspersed cerebral parenchyma. Hematoxylin and eosin stain.

uncle. It continued forward to enter the cerebral parenchyma and terminate in a blind pouchlike ending in the right lateral ventricle (figure 1). Distally the lumen was filled by a red, somewhat friable thrombus and the vessel was perforated on the lateral surface resulting in intraventricular hemorrhage. The paraventricular cerebral tissue adjacent to the site of perforation was fragmented, softened, and hemorrhagic.

Microscopic examination showed the vascular mass to consist of distinct arterial and venous elements. Many of the arteries exhibited fraying and reduplication of the elastic lamellae and both arterial and venous walls were thickened irregularly with fibrous connective tissue. Small islands of cerebral parenchyma exhibiting demyelination and astrocytic proliferation were interspersed between the abnormal vessels (figure 2). Adjacent to the rupture site the lumen of the thin-walled vascular extension was filled with a thrombus exhibiting early organization at the periphery. The media and adventitia were infiltrated in some areas by small aggregates of lymphocytes. The cerebral parenchyma adjacent to the site of vascular rupture exhibited tissue fragmentation, extravasation of red blood cells, and a surrounding area of demyelination. The small blood vessels in this region exhibited adventitial proliferation as well as perivascular collections of lymphocytes and macrophages filled with brown pigment. The cerebral meninges were thickened with loose fibrous connective tissue and contained scattered aggregates of perivascular lymphocytes and plasma cells.

DISCUSSION

Cortical arteriovenous malformations usually present a characteristic symptomatology. Manifestations are rare before the age of ten and commonly first appear in the second and third decades. Convulsions are the most character-

istic symptoms, occurring in more than two-thirds of all cases.[9,10] Intracranial hemorrhage and psychic disturbances each are manifest in approximately half the clinical cases. Headache is common but not characteristic. Bruit is noted occasionally, and dilatation of the scalp and facial veins and exophthalmos are also observed from time to time. Calcification of the lesion was reported in six of 43 cases by Olivecrona and Riives.[10]

Although only 11 cases of arteriovenous malformation of the great vein of Galen appear in the literature, the symptomatology is sufficiently consistent to indicate that it varies significantly from the above described symptom pattern (table 1). Five cases were under five years of age, four being less than 18 months old. Convulsions were of only minor significance, with seizures appearing transiently in two patients during childhood. Hemorrhage occurred in only three cases, while mental or developmental deficiency was noted in five. Hydrocephalus was the most prominent finding, being present in nine of the 11 cases. Dilatation of the scalp and facial veins was reported in five cases. Calcification of the lesion was prominent in the adult cases, as was visual symptomatology. These consisted of paresis of upward gaze, anisocoria, field defects, blurred vision, ptosis, loss of vertical movements, absence of conjugate movements, external strabismus, and inactivity of the pupil to light and accommodation. Epistaxis, hemiparesis, hemianesthesia, paresis of one hand, and excessive fatigue have also been reported in single cases.

TABLE 1

ARTERIOVENOUS MALFORMATION OF THE GREAT VEIN OF GALEN
(11 CASES)

	Age		
	0–5 years	*15–60 years*	*Total*
Cases	5	6	11
Hydrocephalus	5	4	9
Dilated face and scalp veins	4	1	5
Headache	2	3	5
Calcification	0	5	5
Mental or developmental disturbances	2	3	5
Visual disturbance	0	4	4
Bruit	2	1	3
Hemorrhage	2	1	3
Vomiting	1	1	2
Exophthalmos	1	1	2
Dizziness or faintness	1	1	2
Convulsions	0	2	2

The early and unusual symptomatology of arteriovenous malformations of the great vein of Galen appears to be consequent to anatomic position. Hydrocephalus is produced by compression of the aqueduct of Sylvius by the vascular mass. This may appear in infancy and thus account for the early manifestation of the lesion. Pressure on the corpora quadrigemina or adjacent

visual structures is responsible for the visual disturbances. The infrequency of convulsions appears to be due to the lesion's distance from areas more commonly concerned with convulsive activity. The frequency of dilatation of the scalp and facial veins cannot be explained simply. An associated anomaly of vascular drainage of the involved area would be necessary to adequately account for the finding, since the vein of Galen is not directly concerned with scalp or face drainage. The report of Russell and Nevin[1] indicates that such anomalies may be associated with the arteriovenous malformation. The increased incidence of calcification of the lesion is also without adequate explanation.

Large venous channels in direct communication with an artery as well as blindly ending vascular pouches have been described in relation to arteriovenous malformations. It is distinctly unusual for such a vascular pouch or venous channel to rupture intraventricularly at a site distant from the main body of the lesion. Intraventricular rupture of arteriovenous malformations have been reported, however, when a cortical lesion extends deeply to the margin of the lateral ventricle.

SUMMARY AND CONCLUSIONS

1. A case of arteriovenous malformation of the great vein of Galen is described, bringing the total cases reported in the literature to 11.

2. Arteriovenous malformations of the great vein of Galen present a symptomatology differing from that observed with similar lesions in cortical locations. The manifestations often appear earlier in life and hydrocephalus and visual disturbances are frequent. Convulsions and hemorrhages are uncommon.

3. The intraventricular rupture of a venous extension distant from the main body of the lesion is rare.

REFERENCES

1. Russell, D. S., and Nevin, S.: Aneurysm of the great vein of Galen causing internal hydrocephalus: Report of two cases, J. Path. & Bact. 51:375, 1940.
2. Alpers, B. J., and Forster, F. M.: Arteriovenous aneurysm of the great cerebral vein and arteries of the circle of Willis, Arch. Neurol. & Psychiat. 54:181, 1945.
3. Boldrey, E., and Miller, E. R.: Arteriovenous fistula (aneurysm) of the cerebral vein (of Galen) and the circle of Willis, Arch. Neurol. & Psychiat. 62:778, 1949.
4. Jaeger, R., and Forbes, R. P.: Bilateral congenital arteriovenous communication (aneurysm) of the cerebral vessels, Arch. Neurol. & Psychiat. 55:591, 1946.
5. Lumsden, C. E.: A case of aneurysm of the vein of Galen, J. Path. & Bact. 59:328, 1947.
6. Oscherwitz, D., and Davidoff, L. M.: Midline calcified intracranial aneurysm between occipital lobes, J. Neurosurg. 4:539, 1947.
7. Raskin, N.: Angiomatous malformation of the brain, J. Neuropath. & Exper. Neurol. 8:326, 1949.
8. Wolfe, H. R. I., and France, N. E.: Arteriovenous aneurysm of the great vein of Galen, Brit. J. Surg. 37:76, 1949.
9. Olivecrona, H.: Die arteriovenosen Aneurysmen des Gehirns, Deutsche med. Wchnschr. 75:1169, 1950.
10. Olivecrona, H., and Rives, J.: Arteriovenous aneurysm of the brain, Arch. Neurol. & Psychiat. 59:567, 1948.

An Analysis of Agnosia

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THE precise significance of disabilities which are classed as "agnostic" has not yet been determined. A number of definitions of the term "agnosia" exist, but differ widely because of uncertainty of the exact nature of the condition. The term was first proposed by Freud[1] in 1891 to describe patients who had difficulty with "relating of objects to object concepts." Many other authors have written on the subject of agnosia, and an excellent survey of the relevant literature is contained in Nielsen's book *Agnosia, Apraxia, Aphasia.*[2] Nielsen himself defines agnosia as "a disturbance of recognition or identification . . . . which represents a limited loss of function. The limitation cannot be determined unless general cerebral function is fairly well retained." Nielsen quotes the definitions of von Monakow and Dejerine. Von Monakow[3] said, "one understands by the term agnosia a lessening of the power to recognise or to differentiate by their characteristic features through a sense organ otherwise easily recognisable sensory impressions (especially through vision, hearing, touch) in the presence of relative preservation or very slight disturbance of elementary function of the sense organ concerned as well as essentially preserved sensorium and speech." Dejerine[4] defined agnosia as "a difficulty of recognition. Recognition is that psychological phenomenon which permits us by the use of one or other of our senses to identify an object under observation with an object previously observed, and of which we have registered the mental picture in the form of a mental image." Since that time the term has been subjected to great elaboration, so that there exists today a complicated nomenclature of "agnostic" disturbances such as visual, auditory, and tactile agnosias (all of which have been subdivided into such varieties as visual object agnosia, visual verbal agnosia, acoustic musical agnosia, acoustic verbal agnosia, and so on) as well as "finger" agnosia; "right-left" agnosia, autotopagnosia, simultanagnosia, spatial agnosia, and so on. It has even been suggested that a specific area of the cortex controls each separate variety of gnosis and that a lesion of such an area will result in one of the specific disorders listed above. An attempt will be made here to analyze the significance of agnosia and to suggest an underlying disturbance of function common to all the disorders described as agnostic.

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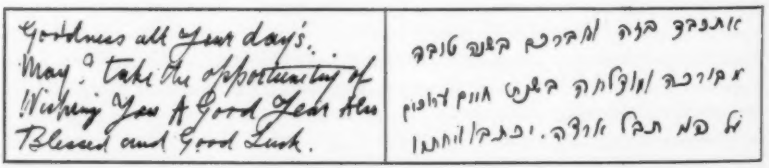
Gnosis, or the recognition of objects and symbols with the help of sensory data, depends upon perception, which is here defined as the qualitative experience of a conscious individual occurring as the result of the unconscious reception, selection, differentiation, and integration of sensory stimuli. The precise nature of sensory stimuli is not known and is irrelevant in this connection. Whatever their nature, sensory stimuli are perceived qualitatively as sensations of seeing, hearing, tasting, feeling, and so on. In a previous paper[5] it was suggested that repeated perceptual experiences form the basis of sensory images, systems of symbols, and abstract thinking. To recapitulate briefly, it was suggested that the human infant first perceives a limited variety of crude sensations, all of which are accompanied by appropriate affective states. The infant is later able to differentiate sensations more finely. For example, visual sensations may be bright or dim, taste may be sweet or salty. When a perception has been repeated, possibly many times, the child is able to abstract the common qualities of all the experiences and learns to recognize them as belonging to a specific situation when they occur in the future.

These common qualities possibly form a specific pattern of cerebral activity and may be called "memory images." Images do not, of course, exist as such in cerebral tissue. They do not exist at all except as temporary qualitative states of mind evoked by immediate patterns of cerebral activity. That is to say, when a certain perceptual situation has been repeated several times, an individual may abstract the common qualities of the patterns of cerebral activity which belong to all the situations. The common patterns may cause him to recall actively, although unconsciously, the qualitative experience of similar past situations. The specific patterns by themselves are meaningless. They acquire significance only in the mind of the individual. The act of remembering is, therefore, not merely a passive association with past experience. It involves active recognition of the patterns of cerebral activity or "memory images." An analogy may be drawn from a machine made in such a way that, if presented with serial information in specific form, it abstracts common patterns and responds accordingly. Before the abstraction and the response can be said to have meaning, however, they must be analyzed or perceived by a human observer in whose mind alone they acquire significance. A "memory image" embodies the whole character of a perceptual experience together with its affective accompaniment. It may belong to any or all sensory categories. It may also be kinesthetic or kinetic involving patterns of sensory-motor behavior. The common qualities of many successive perceptual experiences may then be endowed with specific symbolic representation. Symbols take the form of words, mathematical figures, musical notes, and so on. Symbols permit the elaboration of further systems of abstractions such as algebra, geometry, physics, and so on. Symbols represent compound experience in a condensed form. In addition to the development of symbols and the processes of abstraction, certain other mental performances belong to perception.

It is suggested that sensations are always perceived as possessing spatial location. We recognize sensations as originating either upon or within certain

regions of our bodies (as in the case of touch, pain, postural sensibility, and other "feeling" modalities), or outside our bodies but within limited surroundings in the case of vision, hearing, and smell. Thus all sensations have a spatial quality. This quality is attributed to the sensation by the individual who perceives it. He relates the sensation to a specific situation on or within his own body or in the space beyond his body. A continuous active judgment of relationships is performed. The spatial qualities of sensations immediately perceived, that is, excluding abstract conceptions of space, are strictly related to the individual who perceives them. An individual tends to regard his own body as a structure possessing a central longitudinal axis and two sides, the right and left, on either side of this axis.[6] Immediate space is regarded in the form of two fields which extend on either side of the body and which merge in the midline before and behind. The spatial fields are largely determined by vision, partly by feeling (which includes postural sensibility and touch), and partly by hearing, especially in blind people. Cerebral disease may interfere with the performance of the attribution of spatial qualities to sensations, and certain patients who do appreciate sensations do not perceive them in their correct location. The phenomenon known as "alloesthesia" and visual and tactile disorientation are examples of this difficulty. The agnostic defects are closely connected with the performance of attributing spatial location to sensations, as will be shown later.

Temporal qualities are also attributed to sensations, depending upon the sequence in which they are perceived in relation to one another. Directional qualities are likewise attributed to sensations by the perceiving individual, depending upon both spatial and temporal relationships. For example, an individual in Western countries writes, reads, scans pictures and music from left to right, whereas in the East these activities are performed from right to left. (An example of English and Hebrew writing is seen here):



Reading, writing, the performance of skilled movements, dressing, and many other activities require perpetual judgment of right-to-left, vertical, and horizontal relationships.

Therefore, it is obvious that perception is not a passive process. It demands action on the part of the individual who perceives. Perception thus involves the reception of sensory stimuli, their differentiation and integration, and the allocation of a variety of qualities to sensations by the perceiving man. That the process is not merely one of the associating of sense data with "memory images" was first suggested by Lissauer.[7] It involves spontaneous action each time.

It has been mentioned above that a perceptual experience may include sensations of all categories. It is a multidimensional experience, the result of a total situation at a single moment in time. In practice, the separate sensory qualities of perceptual experiences are not isolated one from another. The single experience may include qualities of sight, sound, touch, and so on, all sensations which are normally endowed with spatial and temporal qualities.

Many sensations are likewise compound experiences. That is, they involve multiple sensory relationships. For example, seeing involves not only pure visual sensation. In order to see the world in a correctly oriented manner, a man must relate visual sensations to postural ones. He must maintain a notion of his position in relation to gravity; this performance involves his vestibular system and vestibulovisual connections. It is well known that vestibular disease causes visual disorder, for example, the sense of objects spinning in a rotary manner experienced in vertigo caused by disturbance of the labyrinth. Similarly, appreciation of postural sensibility in the fingers involves not only awareness of the position of a single joint in space, but the recognition of its position as a whole in relation to the rest of the body and also the relation of the body to gravity. For example, an individual will have to vary his notion of the position of his toes in space according to whether he is standing, or sitting, or lying flat on his back. Therefore, it is obvious that the perceptual process is a very complex one, and each perception is a compound of integrated activity of a physiologic and psychologic nature. It is suggested that the disorders which are described as agnostic are concerned with those aspects of perception which require spontaneous, active, although not necessarily conscious, mental performance on the part of the perceiving individual. The agnostic defects involve processes of abstraction and symbolic representation and the attribution of spatial, temporal, and directional qualities to sensory stimuli. This thesis will now be demonstrated in its application to certain varieties of agnosia.

VISUAL AGNOSIA

When a healthy adult person sees a three-dimensional object, he perceives it against a background, the planes of the object varying in their appearance according to their distance from him and the angle at which they deviate from imaginary vertical and horizontal planes before him. He is aware of the distance of the object from him because of its size in relation to other objects which he has previously experienced in a multisensory manner, for instance, walls, furniture, trees, sky, and buildings. He is aware of the color of the object and its shape. He may be aware of its texture if he has previously touched a similar or the same object. It is suggested that in seeing this object he must actively achieve and maintain a complex performance. He must preserve the relations of the object to the background and to himself and the planes of the object to one another. Failure to do so may result in a variety of visual disturbances. Visual disorientation or loss of three-dimensional vision may occur. If the disorder is sufficiently severe, the object may merge with its

background or become so spatially disordered as to be unrecognizable. That is to say, it will lose its familiar appearance. The patient retains his vision of the object, however, but he is unable to distinguish the object in its relation to the background or to recognize the object. This defect, an agnostic one, is essentially an inability or failure to judge sensory relationships. Similarly, when an individual looks at a two-dimensional pattern, for example a triangle drawn on a page, in order to perceive it as a triangle the relationship of the parts of the figure (the three lines joined in a specific design) must be actively preserved. If this action is not performed correctly, failure to recognize triangularity will occur, although the single components of the figure may be well seen. The notion of triangularity therefore demands an understanding of specific spatial relationships. A woman suffering from effects of a meningioma in the right parietal region of the brain performed as follows when asked to draw a triangle:

She was unable to copy designs correctly or to find her way in familiar places, but she was mentally alert otherwise. It is suggested that these disorders, which represent spatial agnosia, may all be described as inability to judge sensory relationships.

It is possible that a similar state of affairs occurs in certain patients who, because of cerebral lesions, are unable to read, write, calculate, copy drawings, and so on, although other aspects of mental performance are well preserved. According to Dr. J. Purdon Martin (personal communication), certain patients suffering from "word-blindness" are unable to judge geometric spatial relationships of the letters and words.

Patients suffering from "alexia" often attempt to translate the visual sensory performance into a postural or kinesthetic one. One example is shown in a 73 year old right-handed man who, as a result of a lesion in the left cerebral hemisphere, was almost totally unable to read although spoken speech was well preserved. When asked to read a word he attempted to trace the outline of each letter with his finger, repeating the movements again and again in the hope that he might recognize this kinetic image of the letter. Thus he might have been able to substitute postural and kinetic patterns for visual ones and therefore judge the spatial relationships and directional flow of the letters without the aid of vision, like a blind man reading Braille. The famous patient with visual agnosia described by Goldstein and Gelb[8] was said to have been word-blind, but could read if allowed to trace the letters by means of writing movements with his fingers. If, however, a word was crossed out by strokes at random, he was unable to read it. When shown geometric shapes,

or Milontine therapy, the new drugs were added to the patients' previous to recognize them. This behavior illustrates a point which has been emphasized throughout this paper – that perception is a qualitative experience which cannot be quantitatively determined. It is a property of mind, different in character from those phenomena, such as physiologic processes, which can be determined quantitatively. When considering agnosia it is essential to make a distinction between psychologic and physiologic phenomena. Sense data are the basis of perception. The final perception has specific qualities, yet the sense data need not be specific in order to achieve the same qualitative experience. The same perception may sometimes be experienced as a result of visual, auditory, or tactile sensory stimulation. It is probably true to say that the more abstract and highly developed the perception, the more easily may it be obtained by interchangeable sense data or interchangeable symbols. When a patient who suffers from visual agnosia is allowed to hold the object (which he cannot recognize by sight), he is immediately able to recognize it by means of judging the correct sensory relationships with the aid of posture and touch.

TACTILE AGNOSIA OR ASTEREOGNOSIS

The recognition of size, shape, and nature of an object by means of touch and postural sensibility alone requires understanding of the relative positions and directional flow of one plane of the object to another, the whole being mentally integrated in a dynamic equilibrium as a result of the exploration of the moving fingers. A patient suffering from astereognosis may be able to judge certain sensory qualities belonging to the object in his hand, such as temperature and texture, but he is unable to recognize it as a whole. For example, if such a patient is given a nail file in his affected hand, he may be able to judge without seeing it that it is a cold metal object, that there is a sharp point and a rough surface. However, he is unable to integrate spatially the total qualities of the object, to judge the tactile relationship of one quality to another. When he looks at the object he is immediately able to recognize it by means of the visual judgment of relationships.

AUDITORY AGNOSIA

A person suffering from auditory agnosia hears but does not recognize sounds. This disability is possibly the result of a failure to contrast and compare the varying pitch and tone of sounds against preceding and succeeding sounds. A patient suffering from auditory agnosia, while quite unable to understand spoken words, may be perfectly able to comprehend the meaning of written words.

FINGER AGNOSIA AND AUTOTOPAGNOSIA

The patient with "finger agnosia" is fully aware that he possesses hands and fingers, but he is unable to recognize one finger in relation to the others. This disability may be due partly to a failure to understand the concept of

the difference between fingers. If the concept is retained, the disability is due to inability to contrast and compare the fingers, possibly in relation to an imaginary central longitudinal axis in the hand. The condition known as autotopagnosia is similar to finger agnosia. If language is relatively preserved, the patient is aware that he possesses different parts of his body, each of which is symbolized by a specific name. He has great difficulty, however, in recognizing one part in relation to the others.

AGNOSIA FOR "RIGHT AND LEFT"

Difficulty in recognizing "rightness" and "leftness" is probably of two kinds. In one the defect is due to an inability to comprehend the concept of right and left. This disability is often seen in lesions of the major hemisphere. In patients suffering from minor hemisphere lesions, there may often be seen a confusion between right and left. The difficulty here probably arises because the patient is unable to contrast one side against the other. The weakness of one side compared to the other may be the result of a physiologic disturbance. The fact that one side of the body is physiologically weaker than the other, however, does not give rise to right-left disorientation unless an agnostic defect is also present. The agnostic difficulty is therefore superimposed upon the physiologic disturbance. One side of the body is perhaps less well represented mentally than the other, and the patient does not attribute location to stimuli in strict adherence to the normal pattern of right and left contrasts and comparisons. The inability to attribute location is the agnostic defect.

DISCUSSION

Agnostic defects are clearly of a complex nature. The basic disability does, however, involve a failure to compare and contrast sensory relationships. This disability is of a psychologic nature. When disorders of a purely physiologic nature occur, preventing the correct ordering of sensory relationships such as vertigo due to vestibular disease or a hemiparesis, the disorder is not an agnostic one. Similarly, although impairment of vision may prevent recognition of an object, this disability is not agnostic. In agnosia the physiologic components of sensation may indeed be impaired, probably always to a slight extent, but the defect is not sufficient to account for the total disability; nor is agnosia simply a defect of association. Gnosis demands fresh mental activity, not necessarily of a conscious nature. It is a property of mind based on the physiologic integration of sensory stimuli.

It has been mentioned that patients suffering from one variety of agnosia are often able to overcome the disability with the aid of additional sensory information. The patient with visual agnosia is able to recognize objects if allowed to handle them. The patient with auditory agnosia is able to recognize the meaning of written words. He is able to remedy his defect if he can transfer his perceptual activities into a realm where comparison and contrast, or the judgment of sensory relationships, can be effected. Therefore, the patient is not suffering from dementia, nor is he suffering from a purely physio-

logic disturbance. A further distinction may be drawn between agnosia and dementia. The latter condition also involves defective powers of mental performance, but does not basically involve sensation. In agnosia the disability is concerned with perception, the qualitative experience which results from the reception and integration of sensory stimuli, the active recognition of sensory patterns and their endowment with various qualities. Agnosia has its origin in defective perception in this sense and as a rule mainly concerns one category of sense data. Dementia has its origin in defective total mental function, and, as a result, perception may be affected later. If a part of mental activity is disturbed, as occurs in agnosia, mental capacity as a whole must of course be affected, but only partially. The agnostic defects are usually specific and limited. Dementia affects global mental function, and the agnostic-like difficulties which are seen in demented persons are secondary to the disturbance of general mental capacities.

Finally, it is suggested that the varieties of agnosia should not be regarded as well defined, isolated entities of disease process, but as aspects of defective perception. They are all fundamentally the result of the inability or failure of the individual to compare and contrast sensory relationships.

SUMMARY

An attempt has been made to analyze the significance of conditions described as "agnostic." Gnosis involves perception, here defined as the qualitative experience of a conscious individual occurring as a result of the unconscious reception, selection, differentiation, and integration of sensory stimuli. It is pointed out that perception is a process which demands spontaneous action on the part of the individual who perceives. Perception requires the active, although not necessarily conscious, abstraction of sensory patterns and their subsequent active recognition (if they occur again).

All sensations are, in addition, endowed by the perceiving individual with certain qualities of a spatial, temporal, and directional nature. In order to attribute such qualities to sensations, an active judgment of sensory relationships is essential.

It is suggested that agnosia is due to defective ability to judge specific sensory relationships, which is a psychologic disorder. A perceptual experience may involve several or all categories of sensation. The final perception which occurs at a single moment in time is a multidimensional experience. It is based on sensation, but not necessarily on specific sensation.

Patients suffering from one variety of agnosia may be able to overcome their disability with the aid of additional sensory information which permits them to accomplish the judgment of sensory relationships. While the physiologic components of the relevant sensation are often impaired in patients suffering from an agnosia, the defect is as a rule too slight to account for the total disability.

A distinction is drawn between agnosia and dementia. The latter condition involves primarily defective powers of mental performance but does not

basically arise from defective perception. Agnosia has its origin in defective perception and although it is the active mental aspect of the perceptual process which is affected, the disability primarily involves sensation. As a rule, only one category of sensation is affected and other aspects of mental function may be unimpaired. Dementia affects total mental performance.

Finally, it is suggested that the varieties of agnosia, to which a complicated terminology has been applied, should be regarded as aspects of defective perception, all essentially caused by the inability of the individual to compare and contrast sensory relationships of specific categories.

REFERENCES

1. Freud, S.: Zur Auffassung der Aphasien, Leipzig and Vienna, Franz Deutrake, 1891.
2. Nielsen, J. H.: Agnosia, Apraxia, Aphasia, New York, Paul B. Hoeber, Inc., 1946.
3. von Monakow, C.: Die Lokalisation im Grosshirn und der Abbau der Funktion durch Kortikale Herde, Wiesbaden, J. F. Bergmann, 1914.
4. Dejerine, J.: Semiologie des Affections du Systeme Nerveux, Paris, Masson et Cie, 1914.
5. Reinhold, M.: Some clinical aspects of human cortical function, Brain 74:399, 1951.
6. Goodby, W., and Reinhold, M.: Some aspects of human orientation in space, Brain 75: 472, 1952.
7. Lissauer, H.: Ein Fall von Seelenblindheit, Arch. f. Psychiat. 21:222, 1889.
8. Goldstein, K., and Gelb, S.: Zur Psychologie des optischen Wahrnehmungs- und Erkennungsvorganges, Ztschr. f. d. ges. Neurol. u. Psychiat. 41:1, 1918.

Sudden starts or jerks constitute a very common form of *petit mal*, sometimes with loss of consciousness, sometimes without. In the latter case it may be doubted whether they deserve to be ranked as distinct seizures. For instance, one patient who had occasional epileptic fits was liable to these starts every morning, soon after getting up. Both arms jerked suddenly, and apparently the legs also, since, if she was standing at the time, she would fall. Occasionally the start will throw the patient forward on the knees. The start may be followed by transient dullness, though there is no actual loss of consciousness, as in one patient, whose major attacks were severe, and who had minor attacks, one of which I witnessed. She gave a sudden start, put her hand to her head as if in pain, seemed to have a difficulty of speaking for a moment, and then was better. There did not appear to be a moment of actual unconsciousness. Closely allied to the starts is a sudden backward movement. One patient, a girl, had had for fifteen years many attacks every day in which she suddenly took a step or two backward, looking strange for a moment, and immediately was well. She never fell unless there was some object behind her to trip her up. There was complete unconsciousness for the moment. She was never aware of the attack, except by finding that persons near were looking at her in astonishment. I witnessed many of these seizures, and neither I, nor the students who were with me, could ever discern the slightest change of color in the face, which was fairly ruddy. Another patient, in the minor attacks, always suddenly went back, the face was drawn slightly to the right, consciousness was lost for a moment, and then he was better.

W. R. Gowers in *Epilepsy and Other Chronic Convulsive Diseases*, published in 1885.

Mysoline and Milontin

Two New Medicines for Epilepsy

Bushnell Smith, M.D. and Francis M. Forster, M.D.

IT IS NOW nearly a century since Sir Charles Locock[1] introduced the use of bromides in the treatment of epilepsy, constituting the first truly effective anticonvulsant drugs. Since that time there has been a crescendo-like interest in the production and therapeutic trial of increasing numbers of anticonvulsants in each decade. Despite all these efforts, the problem of control of convulsive disorders still remains far from solved. While the majority of the patients now have their seizures alleviated with medication, there is ever greater concern for the successful therapy of that smaller group of uncontrolled epileptic patients. Consequently there is a need for the development of newer and perhaps more efficacious anticonvulsant drugs for the relief of these latter patients.

Two compounds which have become available on an experimental basis within the past two years are 5-phenyl-5-ethyl-hexahydropyrimidine-4:6 dione, or Mysoline, and N-methyl-a-phenyl-succinimide, or Milontin. Mysoline is a white crystalline substance in tablet form containing 250 mg. each; it affords a high protection against electrically-induced convulsions in animals. Milontin is also a white crystalline powder which is supplied in yellow gelatine capsules of 500 mg.; it affords a high protection against Metrazol-induced convulsions in animals.

A preliminary report has been made on results with these drugs,[2] and it is now felt that sufficient time has elapsed to present some conclusions regarding the efficacy and possible future of these two medications.

CLINICAL MATERIAL

The present series consists of 150 patients seen at Georgetown University Hospital and in the Epilepsy Clinic of the District of Columbia Society for Crippled Children. One hundred of these patients were treated with Mysoline and 50 with Milontin. They ranged in age from two months to 55 years. Seventy-five patients were over 14 and 75 under 14 years of age. Seventy-six

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Read before the American League Against Epilepsy August 22, 1953.
This work was supported in part by Public Health Service Grant MH-385.

patients had grand mal or focal convulsive seizures; 84 had one or more types of petit mal seizures; and 50 had psychomotor seizures. Obviously there was a considerable overlap in seizure types. In fact, only 27 of the entire series had one type of seizure alone. Of the 76 patients with major convulsions, 30 had psychomotor seizures also, while 40 had one or more forms of the petit mal triad in addition to the convulsions. One patient had convulsions, psychomotor seizures, and petit mal absences.

On the original visit of each patient to the epilepsy clinic a description of the seizures is obtained, and in addition care is taken to estimate the frequency of each type of seizure, the shortest and longest time intervals between seizures, and the dates of recent attacks. This information is used to determine the efficacy of therapy. No patient is considered seizure-free or seizure-controlled until the time interval since his last seizure has more than doubled the previous longest seizure-free period. Marked improvement is construed as a decrease in seizures from average frequency to one greater than the spontaneous seizure-free period but less than a multiple of it, and with the reappearance of seizures within that range.

Patients who presented themselves for treatment had all been treated previously with standard anticonvulsants with moderate or no success in seizure control. The standard medications (that is, those available in pharmacies and not considered under new and experimental drugs) were continued, and when indicated the dosage was increased in the preliminary trial. Only those patients whose seizures could not be controlled with the standard medications in adequate dosages and without toxic signs were treated with the experimental drugs, Mysoline and Milontin. When it was decided to attempt Mysoline or Milontine therapy, the new drugs were added to the patients' previous medication if the latter was considered to be of slight to moderate benefit. Therefore, no abrupt transition was made from standard medication to new anticonvulsant drugs. Both the standard preparation and new medication were continued and the dosage of the new medication increased as necessary. Once seizure control was obtained by this technic the standard drug was decreased; if seizures returned the dosage of the new medication was increased.

RESULTS OF MYSOLINE THERAPY

Results of Mysoline therapy in the group of 100 patients are shown in table 1. Thirty-three became seizure-free using Mysoline and 36 showed marked improvement. In 12 patients there was only slight improvement, while five showed no change in seizure frequency. In no patients were the seizures increased while on Mysoline therapy. However, in 14 patients toxic signs and symptoms developed which necessitated discontinuing the medication. When these results were examined by seizure types, patients with major convulsions responded well, with 22 (47 per cent) completely controlled and 12 (26 per cent) markedly improved. Of the ten patients with psychomotor epilepsy, four (40 per cent) were completely controlled, while two (20 per cent) showed marked decrease in seizures. In the group with both psychomotor epilepsy

TABLE 1
MYSOLINE THERAPY — 100 PATIENTS

	Petit mal triad		*Grand mal*		*Psychomotor*		*Grand mal and petit mal*		*Grand mal and psychomotor*		
	With	*Without*	*With*	*Without*	*With*	*Without*	*With*	*Without*	*With*	*Without*	
No seizures	1	0	18	4	4	0	3	2	1	0	33
Marked decrease	0	0	12	0	0	2	4	1	15	2	36
Slight decrease	0	1	6	0	1	1	0	0	2	1	12
No effect	1	0	2	0	0	0	1	1	0	0	5
Toxic reaction	2	1	4	1	1	1	0	1	2	1	14
Total	4	2	42	5	6	4	8	5	20	4	100

"With" and "Without" refers to other anticonvulsant medications.

and convulsions, one (4 per cent) was completely controlled while 17 (71 per cent) were markedly improved. In this group convulsions were almost completely eliminated while the psychomotor attacks persisted, although decreased in frequency. The petit mal triad responded poorly to Mysoline, with one patient (16 per cent) completely controlled and none markedly decreased. Among those having convulsions along with one or more forms of the petit mal triad, five (38 per cent) were completely controlled and five (38 per cent) showed a marked decrease.

Of the patients taking Mysoline, 20 required no other anti-epileptic medication. The average dose was 1 gm. a day. Control was reached at 0.5 gm. to 2 gm. a day. The 80 patients receiving the new drug in addition to other medications took an average dose of 750 mg. of Mysoline a day. Effective control was reached on dosages ranging from 500 mg. to 1.5 gm. a day.

As noted above, toxic signs appeared in 14 of the 100 patients to whom Mysoline was administered. These toxic signs bore no relation to the type of seizure under therapy. The toxic manifestations fall into three groups: 1) acute nausea, vomiting, and dizziness; 2) excessive somnolence; and 3) psychiatric difficulty.

Nausea, vomiting, and dizziness are acute manifestations appearing after taking a single dose of Mysoline. They occurred in seven of the 100 patients, four of whom were also severely ataxic. The vomiting may be quite prolonged, and in one of our patients was continuous for four hours. Usually it is somewhat intermittent and lasts from one to 24 hours. Most of these patients refused to take another dose of the medication. However, one patient continued on the medication for a week, during which time she was ataxic and light-headed but the nausea disappeared. Drowsiness also appeared early, usually after the first or second dosage of Mysoline. This occurred in 13 patients in the series, and was so persistent and severe in seven that they requested withdrawal of the drug. Usually the drowsiness disappears after three or four days, and may be compensated for by the use of one of the amphetamines or to some extent by caffeine. There is no relationship to dosage, and sometimes one 250 mg. tablet of Mysoline a day is sufficient to produce drowsi-

ness of this transient nature for three to five days. One patient, however, found that by taking one quarter of a tablet per day for a period of a month she could avoid drowsiness, and the dosage was increased gradually to 500 mg. While severe drowsiness occurred in only 13 patients, most of them had transient drowsiness which disappeared in about a week without the use of amphetamine or withdrawal of medication.

Psychiatric disturbances occurred in two patients and were in the nature of paranoid reaction. One of these instances was particularly interesting, that of a young girl of 16 who, five days after her level of Mysoline was increased above 500 mg. a day, became irritable, irascible, and abusive, suspicious of her parents, and attempted to leave home. When the dosage was reduced to 500 mg. these symptoms disappeared. On three occasions these paranoid, irritable symptoms returned when the dosage was increased. In no instance were any disturbances of hematopoiesis, urinary function, or liver function noted.

RESULTS OF MILONTIN THERAPY

The results of Milontin therapy are presented in table 2. Milontin was given in average daily doses of 2 gm. Significant improvement occurred in 27 of the 50 patients receiving this drug while 12 showed slight improvement, and eight patients showed no effect. In no instance were seizures increased after the administration of Milontin. Six patients with petit mal absence were placed on Milontin therapy. Permanent control of seizures was not obtained in any of these patients, and only one showed marked improvement. All patients showed marked improvement for the first six weeks, but gradually became worse despite large increases in dosage. Myoclonic jerks were present in five patients, and were completely controlled in four. In the six patients with petit mal absence and convulsions only one had complete control and two showed marked improvement. Twenty patients had myoclonic jerks and convulsions, and three showed complete control while ten had marked improvement. Because of this apparent discrepancy, the electroencephalograms were reviewed. Milontine appeared to have little or only a short-acting effect on the pure three per second spike and wave formations, while the patient with the two to four per second slow spike wave or multiple spike and wave responded to Milontin.

Toxic reactions were virtually absent among patients receiving Milontin therapy. Minor transitory rashes of a morbiliform type were encountered in two patients, and excessive drowsiness was seen in one patient. The rash almost invariably cleared quickly on cessation of medication, and resumption of Milontin therapy was not associated with the reappearance of the rash except in one patient who twice developed a morbiliform rash when given the drug. There was some concern regarding this patient's allergic manifestations because she had previously developed leukopenia on Tridione therapy. She was started on desensitizing doses of 10 mg. of Milontin per day. This was gradually increased until she attained an effective anticonvulsant dosage of 2.5 gm. per day without recurrence of a rash and without the development of leukopenia.

TABLE 2
MILONTIN THERAPY — 50 PATIENTS

	Petit mal triad		*Grand mal*		*Grand mal and petit mal*		*Grand mal and psychomotor*		
	With	*Without*	*With*	*Without*	*With*	*Without*	*With*	*Without*	
No seizures	2	2	0	0	1	3	0	0	8
Marked decrease	2	0	2	2	8	4	1	0	19
Slight decrease	1	0	1	1	3	4	1	1	12
No effect	1	2	0	0	0	2	1	2	8
Toxic reaction	0	1	0	0	1	1	0	0	3
Total	6	5	3	3	13	14	3	3	50

"With" and "Without" refers to other anticonvulsant medications.

An interesting and provocative observation was made in patients with brain damage. Twenty-three children who were diagnosed as having "cerebral palsy" in addition to epilepsy became more alert and quieter on Milontin therapy. These, of course, were not striking results in the sense that there was a marked increase in their mental abilities, but both teachers and parents reported independently on this factor. The parents noticed that these children were more amenable at home; the teachers found them better adjusted with the group in class and there was improvement in their ability in the classroom, indicating that this was not a sedative effect. Therefore these children did not appear to be better behaved because they were sleepy, but actually seemed to do somewhat better. This result is not commensurate with seizure control. In three cases seizures were not improved, but the behavioral aspects were much ameliorated.

DISCUSSION

The ideal anticonvulsant drug would be one which would control all seizures equally well, be simple to administer and free of toxic effects. It is extremely unlikely that these criteria will ever be met. At least at the present time such an outlook is not foreseeable. These two new drugs, however, have much to recommend them. Mysoline has shown considerable efficacy in control of all types of seizures, but its major efficacy is in the range of convulsions. This effect has been previously reported.[2–4] However, the results of treatment of psychomotor seizures with or without other types of seizures were also encouraging. It is our opinion that Mysoline is preferable to Phenurone in the treatment of psychomotor epilepsy, and that the latter should be reserved for those patients with psychomotor epilepsy who are not controlled on hydantoinate, phenobarbital, or Mysoline therapy. While Phenurone has a somewhat higher rate of efficacy than Mysoline, the complications attending its use are so much more severe that there is little reason for using it until Mysoline has been found wanting in the individual patient.

The toxic effects of Mysoline, while statistically significant, are for the most part not serious and of transitory nature. The only exceptions to this are the two instances of paranoid trend, and fortunately these disappeared on cessa-

tion of medication. The other toxic symptoms, while discomforting, in no way endanger the patients. Smith and McNaughton[4] reported that patients could continue taking Mysoline after disappearance of nausea, vomiting, dizziness, and ataxia. This, however, has not been our experience, since we have found it very difficult to convince these patients to take the second dose of Mysoline after the first one had precipitated the acute distress. While Mysoline is far from the ideal anticonvulsant, it does have the ability to counteract all kinds of seizures, although with varying degrees of success. While it is toxic, its side effects are not serious and therefore of minor significance.

Milontin, on the other hand, is a specific kind of anticonvulsant with its particular efficacy in the realm of petit mal triad; it is especially effective for patients who have myoclonic jerks. It has little if any effect on convulsive or psychomotor seizures, and when there is a therapeutic efficacy in this realm it is usually because seizures in these patients begin with a petit mal attack. Zimmerman found that Milontin therapy could result in consistent long-term control of petit absences.[5] We have been unable to confirm this, although, in our preliminary report, we too thought that long-term control was possible. This discrepancy may be due to the transitory effect of Milontin on seizures which originate in temporal lobe discharges or which are characterized by the three per second wave and spike formation in the electroencephalogram. As noted before, patients whose dysrhythmias vary from two to four per second are more apt to be treated successfully. Milontin is also free of severe toxic manifestations, and while occasional skin eruptions and somnolence were noted, no serious effects were encountered in any of our patients. Urinary changes reported by Millichap[6] did not occur in our series of cases.

SUMMARY

Both Mysoline and Milontin are effective anticonvulsants. Mysoline comes closest to being an all purpose anticonvulsant, while Milontin is specifically valuable in treating petit mal seizures and myoclonic jerks. No serious toxicity was encountered with either drug.

Mysoline and Milontin for this study were kindly supplied by Ayerst, McKenna & Harrison, Ltd. and Parke Davis Company, respectively.

REFERENCES

1. Locock, C., quoted by Sieviking, E.: Analysis of fifty-two cases of epilepsy observed by the author, Lancet 1:527, 1857.
2. Smith, B., and Forster, F. M.: The role of some experimental anti-convulsants: Mysoline, Milontin and 1461L, M. Ann. District of Columbia 22:279, 1953.
3. Handley, R., and Stuart, A. S. R.: Mysoline: a new drug in the treatment of epilepsy, Lancet 1:742, 1952.
4. Smith, B. H., and McNaughton, F. L.: Mysoline: A new anticonvulsant drug. Its value in refractory cases of epilepsy, Canad. M.A.J. 68:464, 1953.
5. Zimmerman, F. T.: Use of methylphenylsuccinimide in treatment of petit mal epilepsy, Arch. Neurol. & Psychiat. 66:156, 1951.
6. Millichap, J. G.: Milontin: A new drug in the treatment of petit mal, Lancet 2:907, 1952.

A Note on the Reliability of Electroencephalographic Judgments

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THE IMPORTANCE of electroencephalography is illustrated by its widespread use in both diagnostic and research studies. On the basis of available estimates[1,2] we can surmise that 1000 articles on the subject have appeared, including several very careful evaluations of the technic's applicability and shortcomings.[3–5] Nevertheless, only a very few have touched upon the important problem of reliability,[1,6–8] and none has examined the reliability among judges using the same records.

Because of the important bearing of reliability upon the validity of a measuring instrument,[9] the present study has been undertaken. This preliminary investigation deals with the agreement among neurologists as to the presence or absence of pathologic signs in a hospital sample of electroencephalographic records.

Reliability refers to the similarity of results of a measuring instrument upon several applications to the same material, or to the similarity of the results of judges' ratings of the same material. In this case we are concerned with the extent of agreement among several raters looking at the same material, upon whose judgments the diagnostic and prognostic usefulness of the records is based.

Validity refers to the extent to which a measure actually does what it purports to do. High reliability, that is, high agreement on what a scale means, is required before one can test how well a tool measures what its proponents say it measures. We must first ascertain that high agreement on interpretation exists before we can begin to hope that the interpretations themselves are a valid measure.

METHODS AND MATERIALS

A sample of consecutive electroencephalographic records was obtained from ten routinely-referred patients at a Veterans Administration general hospital. These referrals to the neuropsychiatric service were based upon the admission diagnosis as made by the medical officer of the day. All patient

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referrals were suspected of central nervous system involvement. Postexperimental analysis reveals that the final diagnosis on nine out of the ten included a neurologic disorder, and eight of these were central nervous system disorders.

The electroencephalograph was a Grass Model 3C using monopolar and bipolar leads with 16 lead placement. The number and type of records obtained on each patient were as follows: three two-minute monopolar runs; three two-minute bipolar runs; a two-minute survey; a three-minute hyperventilation; and a two-minute clear survey.

Five judges were asked to examine the records and make judgments concerning evidence of pathology and localization. Three of the judges were diplomates in neurology, one not a diplomate but chief of a department of neurology and psychiatry, and one a certified neurosurgeon. Four of the five were members of one or more electroencephalographic societies. Three had been interpreting electroencephalograms for over ten years, one for over five years, and one for over three years. Four of the five have published or are publishing articles dealing with the subject.

Each neurologist was given the complete sets of records for all patients. Each judge was told where the records had been taken and by whom. It was unnecessary to describe in detail the recording technic, for all judges were familiar with the apparatus of the recording laboratory and technician's methods. They were asked to check on cards the appropriate category or categories, as follows: normal, borderline, and abnormal; also focal or general. They were told that a specific diagnosis was optional and that judgments would be anonymous.

RESULTS

The distribution of judgments of the five electroencephalographers for the ten sets of records is given in table 1. There was complete agreement by the

TABLE 1

DISTRIBUTION OF JUDGMENTS OF FIVE NEUROLOGISTS ON TEN EEG RECORDS

	Pathology			*Localization*		
Record	*Normal*	*Borderline*	*Abnormal*	*Focal*	*General*	*Focal and General*
a	5					
b	2	2	1		3	
c	4	1		1		
d	1	1	3	3		1
e	3	2			2	
f			5	2	1	2
g			5	3	1	1
h			5	1	3	1
i	2	3		2	1	
j		2	3	2	1	2

five judges on four of the records as to evidence of pathology. On three more, four of the five judges agreed on evidence of pathology. With respect to localization, all judges agreed on three sets of records, and four agreed on one additional set of records. On localization a "normal" record was presumed "general," but not tallied in the table as such. The category "general and focal" was spontaneously added by certain of the judges who checked both "focal" and "general."

INTERPRETATION

The data indicate relatively low agreement among the diagnosticians. The percentage of complete agreements is only 40 for the presence or absence of pathology indicators; only 30 for localization; and only 10 for the combined categories of localization and pathology. Even when complete agreements and agreements of four of the five judges are combined, the percentage is increased merely to 50 for pathology indicators, 40 for localization, and 20 for both categories combined.

If results such as these are typical where the electroencephalogram is similarly employed in diagnostic and research procedures, one may well question some contemporary estimates of the validity of the technic.[2] Further question as to validity can be raised by examining the reliability of records taken from the same individual. Studies by Travis and Gottlieber[6] and Davis and Davis[7] indicate relatively high consistency, but reference to an article by Gibbs[1] and a study by Hadley[8] casts serious doubt on the record reliability. With questionable reliability for individual records coupled with the low interjudge reliability as suggested by this study, it would appear that careful appraisal of electroencephalographic validity claims is warranted. The results of this preliminary study indicate the necessity for more extensive research on electroencephalographic reliability.

SUMMARY AND CONCLUSIONS

Ten sets of electroencephalographic records from routine admissions to a Veteran's Administration hospital have been studied by five neurologists to determine agreement as to presence or absence of pathology as well as localization of lesions. The percentage of complete agreement on pathology was found to be 40, on localization 30, and on both combined 10. This low reliability of judgments by five experienced neurologists suggests caution in accepting electroencephalographic validity, and points to the need for further research.

COMMENT BY DR. ROBERT B. AIRD

Comparison of interpretations of a given number of electroencephalographic records by a series of electroencephalographers should in no sense be considered a test of the validity of electroencephalography. Rather it is a test of the relative homogeneity of the background and training of the electroencephalographers concerned, and this latter is known to vary consider-

ably. The validity of electroencephalography as a clinical diagnostic tool must be based upon a comparison of interpretations with established facts in the given patients tested, as determined by other diagnostic tests (clinical studies, pneumoencephalography, arteriography, and so on) or pathology (as obtained at surgery or autopsy).

The technic used in the record submitted is different from that used at the University of California and again differs from that used in many other laboratories. In many instances where the findings are not gross, the technic used is not adequate for the determination of focal changes.

COMMENT BY THE AUTHOR

It is agreed that this study is not designed to test the validity of the electroencephalogram, and that the lack of uniform interpretation may well be a test of the homogeneity of the training of the judges. For the purposes of this study no attempt has been made to assess the training of the electroencephalographers employed. However, the factor of possible differential training poses a problem by demonstrating the lack of standards and criteria to be employed in training in electroencephalographic methodology. Such disagreement would imply the lack of strong background research which could provide clinically and experimentally valid standards, and suggests caution in the use and interpretation of the technic.

Concerning the relationship of the electroencephalogram to other technics, as suggested by Dr. Aird, it is to be noted that the record may be consistent with other more reliable and valid indicators and still be judged unreliably; and conversely it may not be consistent with "outside" evidence but still it may be judged reliably.

Considering the criticisms of recording technic, this again points up an area where further research is evidently needed. It would appear that when a standardized technic is acceptable to some eminent neurologists and unacceptable to others, further investigation is in order.

The author gratefully acknowledges the cooperation and assistance of Dr. Friedlander of the department of neurology and psychiatry at Ft. Miley Veterans Hospital, San Francisco, California, as well as that of the other participating neurologist judges.

REFERENCES

1. Gibbs, F. A.: Diagnostic and prognostic value of the encephalogram, J.A.M.A. 118:216, 1942.
2. Lindsley, D. B.: Electroencephalography, in Hunt, J. U., ed.: Personality and the Behavior Disorders, New York, Ronald Press, 1944, pp. 1033-1106.
3. Grinker, R. R., and Serota, H. M.: The present status of electroencephalography in clinical diagnosis, Dis. Nerv. System 2:276, 1941.
4. Davis, P.: Technique and evaluation of the electroencephalogram, J. Neurophysiol. 4:92, 1941.
5. Walter, W. G.: Critical review: The technique and application of electroencephalography, J. Neurol., Neurosurg. & Psychiat. 1:359, 1938.
6. Travis, L. E., and Gottlieber, A.: How consistent are an individual's brain potentials from day to day? Science 85:223, 1937.
7. Davis, H., and Davis, P. A.: Action potentials of the brain in normal states of cerebral activity, Arch. Neurol. & Psychiat. 36:1214, 1936.
8. Hadley, J. M.: Some relationships between electrical signs of central and peripheral activity, J. Exper. Psychol. 27:640, 1940.
9. McNemer, Q.: Psychological Statistics, New York, Wiley and Sons, 1949.

Rehabilitation in Chronic Neurologic Disease

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In 1946 the neurology department of the Minneapolis Veterans Hospital began a program of rehabilitation for patients with chronic neurologic disorders. A partial evaluation of the first four and a half years' activity is presented in this paper.

Fundamentally the rehabilitation program involved the following phases: 1) total evaluation of the patient, including medical, neurologic, psychiatric, social, and vocational status; 2) setting a treatment goal based on these evaluations; and 3) institution of a treatment procedure to achieve this goal.

Aside from specific medical and neurologic therapies the technics employed involved physical therapy, corrective therapy, occupational, social, and vocational therapy, and speech therapy when indicated. The general objectives were improvement in self care, ambulation, and social adjustment.

The ultimate goal varied greatly from one patient to another. In the aged and severely disabled it was necessary to set a more limited objective than in the young individual for whom a goal of greater or lesser economic independence could be achieved. Keeping in mind the physical limits of the patient and the social and economic possibilities involved, a coordinated program was instituted under the supervision and guidance of a single individual, the physician in charge of the patient. All of the various therapies employed were constantly evaluated and supervised.

METHOD AND MATERIAL

Adequate records of 466 male patients who had reached a point of maximum rehabilitation were available for analysis. The point of maximum rehabilitation was defined as the greatest degree of self care and ambulation that could be obtained at the time of discharge from the hospital and the maximum vocational and social adjustment that could be accomplished within the patient's home environment, or a plateau of those physical abilities beyond

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Reviewed in the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the author are the result of his own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

TABLE 1

VETERANS ADMINISTRATION ACTIVITY RATING FORM

Score Four Points for Each Activity

SELF CARE		AMBULATION	
1.	Change position in bed.	1.	Arise & stand w/aid in par. bars
2.	Feed self	2.	Arise & stand w/o aid in par. bars
3.	Wash hands and face	3.	Shift weight from foot to foot in parallel bars
4.	Brush teeth and comb hair	4.	Walk in par. bars with assistance
5.	Write name and address	5.	Walk in par. bars w/o assistance
6.	Use telephone	6.	Walk with assistance of Instr.
7.	Sit up for six hours	7.	Walk w/o assistance, Instr. by side
8.	Get from lying to sitting pos'n.	8.	Arise to stand from w/chair w/o aid
9.	From sit on bed to stand	9.	Walk alone using crutch
10.	Tie pajama bottoms	10.	Climb stairs with railing
11.	Put on & take off shoes	11.	Climb stairs w/rail backwards
12.	From bed to w/chair to bed	12.	Walk sidewards & backwards
13.	Sit and arise from armless chair	13.	Walk alone using cane
14.	Put on & take off pajama bottom	14.	Walk on ground & carpeting (rugs)
15.	Put on & take off pajama tops	15.	Open and close door from stand
16.	In and out of chair at table	16.	Climb bus steps
17.	Shave self	17.	Climb curb
18.	Pick object off floor	18.	Climb steps w/o hand rail
19.	Use toilet w/o assistance	19.	Discard wheel chair
20.	In and out of car	20.	1 point for following distances:
21.	Tie shoes	21.	25 / 50 / 75 / 100 / 150 / 200
22.	Put on and take off braces	22.	300 / 400 / 500 / 600 / 700 / 800
23.	Clothe self completely	23.	1 point for following times--48 ft.
24.	Take bath w/o assistance	24.	85 / 80 / 75 / 70 / 65 / 60
25.	Get from floor to stand	25.	50 / 45 / 40 / 35 / 30 / 25

Date						
Self Care						
Ambulation						
Date						
Time						

which no further improvement could be made in spite of intensive therapy.

The definition and institution of a treatment procedure resulted in empirical division of patients into six treatment groups. Each group required a treatment procedure which, while employing some technics common to all groups, varied in accordance with the clinical syndrome. These various symp-

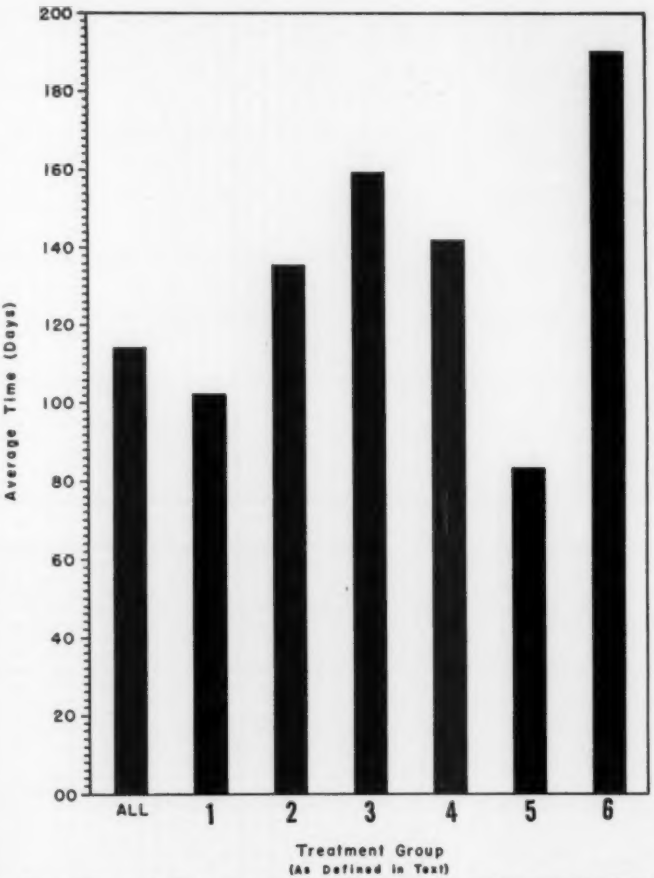

FIG. 1. Time required to reach maximum rehabilitation among various groups of patients.

tom and syndrome groups were the following: 1) hemiplegia, 2) ataxia, 3) disseminated central nervous system lesions, 4) extrapyramidal disease, 5) flaccid paralyses, and 6) paraplegia.

An objective method for measuring progress in accomplishing movements and activities necessary for self care and ambulation was devised. This provided a scoring method, which could be rather directly related to the patient's progress in the rehabilitation program. The activities of self care included washing, dressing, feeding, and toilet care. Ambulation activities included walking, climbing stairs, and crossing the street. The assigned score for each of these activities is determined according to the procedure and index de-

TABLE 2

DISTRIBUTION OF PATIENTS ACCORDING TO FINAL ABILITY POINTS FOR AMBULATION AND SELF CARE BY TREATMENT GROUP, AGE, AND INITIAL ABILITY POINTS

Class	Age	Total	Self Care														Total	Ambulation													
			Initial Ability Points															Initial Ability Points														
			0–25				26–50				51–75				76–100			0–25				26–50				51–75				76–100			
			Final Ability Points															Final Ability Points														
			0–25	26–50	51–75	76–100	0–25	26–50	51–75	76–100	0–25	26–50	51–75	76–100	0–25	26–50	51–75	76–100		0–25	26–50	51–75	76–100	0–25	26–50	51–75	76–100	0–25	26–50	51–75	76–100	0–25	26–50	51–75	76–100
All Classes	All Ages	466	125				88				86				167			466	255				35				31				145		
			24	25	23	53	1	9	16	62	0	0	8	78	0	0	0	167	44	24	32	155	0	1	5	29	0	0	3	28	0	0	0	145
	20–29	68	9				15				13				31			68	29				7				5				27		
			3	2	1	3	0	0	3	12	0	0	0	13	0	0	0	31	6	2	2	19	0	0	3	4	0	0	1	4	0	0	0	27
	30–39	48	6				5				9				28			48	19				3				2				24		
			0	2	1	3	0	0	1	4	0	0	2	7	0	0	0	28	3	2	1	13	0	1	0	2	0	0	0	2	0	0	0	24
	40–49	48	11				9				9				19			48	26				5				2				15		
			0	2	0	9	0	1	1	7	0	0	0	9	0	0	0	19	1	3	3	19	0	0	0	5	0	0	0	2	0	0	0	15
	50–59	217	66				44				41				66			217	129				14				14				60		
			13	10	13	30	1	5	10	28	0	0	4	37	0	0	0	66	22	11	15	81	0	0	2	12	0	0	1	13	0	0	0	60
	60–69	65	27				8				12				18			65	40				4				7				14		
			8	5	7	7	0	1	0	7	0	0	2	10	0	0	0	18	11	5	5	19	0	0	0	4	0	0	1	6	0	0	0	14
	70+	20	6				7				2				5			20	12				2				1				5		
			0	4	1	1	0	2	1	4	0	0	0	2	0	0	0	5	1	1	6	4	0	0	0	2	0	0	0	1	0	0	0	5
Class 1	20–29	22	2				5				2				13			22	6				1				3				12		
			0	0	0	2	0	0	1	4	0	0	0	2	0	0	0	13	0	1	0	5	0	0	0	1	0	0	0	3	0	0	0	12
	30–39	24	5				3				6				10			24	10				3				1				10		
			0	1	1	3	0	0	0	3	0	0	1	5	0	0	0	10	1	1	0	8	0	1	0	2	0	0	0	1	0	0	0	10
	40–49	25	9				5				6				5			25	16				3				0				6		
			0	1	0	8	0	0	0	5	0	0	0	6	0	0	0	5	0	1	3	12	0	0	0	3	0	0	0	0	0	0	0	6
	50–59	139	50				31				31				27			139	91				9				10				29		
			6	7	11	26	0	4	5	22	0	0	2	29	0	0	0	27	8	10	10	63	0	0	2	7	0	0	1	9	0	0	0	29
	60–69	49	24				6				9				10			49	33				4				5				7		
			8	4	5	7	0	0	0	6	0	0	1	8	0	0	0	10	9	5	4	15	0	0	0	4	0	0	0	5	0	0	0	7
	70+	18	6				6				2				4			18	11				2				1				4		
			0	4	1	1	0	2	1	3	0	0	0	2	0	0	0	4	1	1	6	3	0	0	0	2	0	0	0	1	0	0	0	4
Class 2	20–29	9	2				2				2				3			9	5				2				0				2		
			1	1	0	0	0	0	0	2	0	0	0	2	0	0	0	3	2	0	0	3	0	0	0	2	0	0	0	0	0	0	0	2
	30–39	2	1				1				0				0			2	2				0				0				0		
			0	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
	40–49	6	1				1				0				4			6	1				2				0				3		
			0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	4	0	1	0	0	0	0	0	2	0	0	0	0	0	0	0	3
	50–59	16	2				2				4				8			16	9				1				1				5		
			1	1	0	0	0	0	0	2	0	0	0	4	0	0	0	8	1	1	0	7	0	0	0	1	0	0	0	1	0	0	0	5
	60–69	0	0				0				0				0			0	0				0				0				0		
			0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	70+	0	0				0				0				0			0	0				0				0				0		
			0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

TABLE 2 — (Continued)

TABLE 2 — (Continued)

Class & Age		Total	Self Care					Total	Ambulation				
Class 3	20–29	3	0	0	2	1		3	1	0			
			0 0 0 0	0 0 0 0	0 0 0 2	0 0 0 1			0 0 0 1	0 0 0 1	0 0 0 0	0 0 0 1	
	30–39	8	0	0	1	7		8	2	0	1	5	
			0 0 0 0	0 0 0 0	0 0 1 0	0 0 0 7			0 1 0 1	0 0 0 0	0 0 0 1	0 0 0 5	
	40–49	3	0	1	1	1		3	3	0	0	0	
			0 0 0 0	0 1 0 0	0 0 0 1	0 0 0 1			1 0 0 2	0 0 0 0	0 0 0 0	0 0 0 0	
	50–59	12	3	5	0	4		12	9	1	0	2	
			2 0 1 0	1 1 1 2	0 0 0 0	0 0 0 4			5 0 3 1	0 0 0 1	0 0 0 0	0 0 0 2	
	60–69	1	1	0	0	0		1	1	0	0	0	
			0 0 1 0	0 0 0 0	0 0 0 0	0 0 0 0			1 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	
	70+	0	0	0	0	0		0	0	0	0	0	
			0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0			0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	
Class 4	20–29	1	0	0	0	1		1	0	0	0	1	
			0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 1			0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 1	
	30–39	1	0	0	0	1		1	0	0	0	1	
			0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 1			0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 1	
	40–49	3	0	0	0	3		3	1	0	0	2	
			0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 3			0 0 0 1	0 0 0 0	0 0 0 0	0 0 0 2	
	50–59	28	7	2	2	17		28	8	2	1	17	
			2 2 1 2	0 0 2 0	0 0 0 2	0 0 0 17			4 0 0 4	0 0 0 2	0 0 0 1	0 0 0 17	
	60–69	10	2	2	0	6		10	3	0	1	6	
			0 1 1 0	0 1 0 1	0 0 0 0	0 0 0 6			0 0 1 2	0 0 0 0	0 0 1 0	0 0 0 6	
	70+	2	0	1	0	1		2	0	0	0	1	
			0 0 0 0	0 0 0 1	0 0 0 0	0 0 0 1			0 0 0 1	0 0 0 0	0 0 0 0	0 0 0 1	
Class 5	20–29	21	2	5	3	11		21	9	1	0	11	
			1 0 1 0	0 0 2 3	0 0 0 3	0 0 0 11			3 0 1 5	0 0 1 0	0 0 0 0	0 0 0 11	
	30–39	11	0	0	1	10		11	3	0	0	8	
			0 0 0 0	0 0 0 0	0 0 0 1	0 0 0 10			0 0 0 3	0 0 0 0	0 0 0 0	0 0 0 8	
	40–49	10	1	1	2	6		10	4	0	2	4	
			0 0 0 1	0 0 0 1	0 0 0 2	0 0 0 6			0 0 0 4	0 0 0 0	0 0 0 2	0 0 0 4	
	50–59	16	2	4	1	9		16	7	1	2	6	
			0 0 0 2	0 0 2 2	0 0 1 0	0 0 0 9			1 0 2 4	0 0 0 1	0 0 0 2	0 0 0 6	
	60–69	5	0	0	3	2		5	3	0	1	1	
			0 0 0 0	0 0 0 0	0 0 1 2	0 0 0 2			1 0 0 2	0 0 0 0	0 0 0 1	0 0 0 1	
	70+	0	0	0	0	0		0	0	0	0	0	
			0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0			0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	
Class 6	20–29	12	3	3	4	2		12	8	2	2	0	
			1 1 0 1	0 0 0 3	0 0 0 4	0 0 0 2			1 1 1 5	0 0 2 0	0 0 1 1	0 0 0 0	
	30–39	2	0	1	1	0		2	2	0	0	0	
			0 0 0 0	0 0 0 1	0 0 0 1	0 0 0 0			1 0 0 1	0 0 0 0	0 0 0 0	0 0 0 0	
	40–49	1	0	0	0	0		1	1	0	0	0	
			0 0 0 0	0 0 1 0	0 0 0 0	0 0 0 0			0 1 0 0	0 0 0 0	0 0 0 0	0 0 0 0	
	50–59	6	2	0	3	1		6	5	0	0	1	
			2 0 0 0	0 0 0 0	0 0 1 2	0 0 0 1			3 0 0 2	0 0 0 0	0 0 0 0	0 0 0 1	
	60–69	0	0	0	0	0		0	0	0	0	0	
			0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0			0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	
	70+	0	0	0	0	0		0	0	0	0	0	
			0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0			0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	

scribed in previous publications.[1] The form for scoring is indicated in table 1. The score for each item of activity is given when the movement is actually accomplished, regardless of the lack of skill in performance. Most items are dual, for example, put on and take off shoes, and if half of the activity is accomplished the item is given a half score. In this way, a more objective scoring method was achieved, not based on subjective evaluation of degree of skill. These activities may be achieved though there may remain a severe motor disability; therefore, the measure of increased strength in muscle groups frequently reported as improvement in rehabilitation may be questioned. It is customary for the patient to remain in the hospital until he has reached either a maximal level of performance which includes all self care activities without aid, or has ceased to improve in spite of the intensive rehabilitation program.

Parallel with the physical and medical therapies, a program of psychologic, social, and vocational evaluation is maintained. From the moment the patient arrives in the hospital, both he and his family are oriented to a goal of returning to the home environment rather than continued hospital maintenance.

RESULTS

The time required to reach maximum rehabilitation is shown in figure 1. For the total group, the average time was 113.3 days. The group with paraplegia required the longest period of hospitalization, averaging 190.9 days. The group with flaccid paralyses required the least time, averaging 83.4 days. The hemiplegic group, which is the largest and most representative sample, averaged 102.4 days. With respect to age, there were no significant changes in the various decades for the total or any subgroup.

Table 2 presents an analysis of the gain in self care and ambulation in respect to 1) the clinical treatment group, 2) the age of the patient, and 3) the initial level of self care and ambulation ability prior to treatment. The table is unavoidably complex when four variables must be considered; also, to make these tables entirely valid a much larger total and individual sample in each treatment group would be necessary.

A further explanation of the table may be indicated. The table is divided into two major sections: self care and ambulation. Each treatment subgroup is divided into four levels according to the initial ability in self care and ambulation at the time of entrance upon the rehabilitation program (0 to 25, 26 to 50, 51 to 75, and 76 to 100, as derived from the previously mentioned scoring sheet – table 1). The number of patients in each of these four initial ability levels is indicated by the single number in the center of the upper portion of the horizontal division. The numbers below represent the progress made by each of the patients when again classified into the usual four groups for level of ambulation and self care. To demonstrate this, if one considers the treatment class 1 and the age group 50 to 59, there were 139 patients in this group on the rehabilitation program. Fifty of these patients had an initial

TABLE 3
DISTRIBUTION OF PATIENTS ACCORDING TO TREATMENT GROUP, AGE, AND DISPOSITION

Class	Age	Total	Hosp	Dom	Died	Home
All Classes	All Ages	466	6	51	22	387
	20–29	68	0	2	3	63
	30–39	48	0	2	1	45
	40–49	48	2	5	1	40
	50–59	217	2	30	9	176
	60–69	65	1	7	6	51
	70+	20	1	5	2	12
Class 1	20–29	22	0	1	0	21
	30–39	24	0	2	1	21
	40–49	25	0	4	1	20
	50–59	139	1	16	4	118
	60–69	49	1	6	6	36
	70+	18	1	4	2	11
Class 2	20–29	9	0	0	1	8
	30–39	2	0	0	0	2
	40–49	6	1	0	0	5
	50–59	16	0	5	1	10
	60–69	0	0	0	0	0
	70+	0	0	0	0	0
Class 3	20–29	3	0	0	0	3
	30–39	8	0	0	0	8
	40–49	3	1	0	0	2
Class 3	50–59	12	1	1	1	9
	60–69	1	0	1	0	0
	70+	0	0	0	0	0
Class 4	20–29	1	0	0	0	1
	30–39	1	0	0	0	1
	40–49	3	0	0	0	3
	50–59	28	0	6	2	20
	60–69	10	0	0	0	10
	70+	2	0	1	0	1
Class 5	20–29	21	0	1	1	19
	30–39	11	0	0	0	11
	40–49	10	0	0	0	10
	50–59	16	0	0	1	15
	60–69	5	0	0	0	5
	70+	0	0	0	0	0
Class 6	20–29	12	0	0	1	11
	30–39	2	0	0	0	2
	40–49	1	0	1	0	0
	50–59	6	0	2	0	4
	60–69	0	0	0	0	0
	70+	0	0	0	0	0

Hosp. — hospitalized. Dom. — require domiciliary care.

self care ability score of 0 to 25 points. After completing the rehabilitation program, six patients showed no change in their point score. Seven patients progressed to the 26 to 50 point score level. Eleven patients progressed to the 51 to 75 point score level. Twenty-six patients progressed to the 96 to 100 point score ability level. Similar calculations may be made in each class and decade. From these figures one may infer some prognosis as to what may be accomplished or expected of the individual patient in regard to his major functional disability, his age, and the degree of his abilities in self care and ambulation as he begins the program of neurologic rehabilitation.

Considering progress in the total group of those who had an initial minimum self care ability, that is, a point score of less than 25, 24 patients (19.4 per cent) made no gain. In the groups with greater than minimum initial self care, there were, as expected, progressively less failures to make any gain.

In those patients with minimum ambulation ability, 44 (17.2 per cent) failed to gain and overall there was a greater gain relative to the initial ability than was seen in self care abilities.

In the hemiplegic group, statistically the most valid, there was only one failure to achieve maximal self care activity in the third decade age group and all achieved full ambulation. In the fourth decade, 8 per cent failed to achieve complete self care and ambulation. In the fifth, sixth, seventh, and

eighth decades, the percentage failing to achieve full self care and ambulation rose from 25 to a maximum of 44 per cent. However, only a point score less than 50 in either of these categories would be cause to require permanent hospital or domiciliary care. Therefore only the sixth, seventh, and eighth decades presented any true failures in significant numbers of patients, and this number is small. The age factor was much less significant in all other treatment groups, with the exception of the extrapyramidal syndrome group which had similar percentages.

Considering each treatment group separately, the greatest number of failures in both self care and ambulation appeared in the group with disseminated central nervous system lesions and the least in the group with flaccid paralysis. The greatest overall improvement in both self care and ambulation also occurred in the latter group.

The final disposition of the total and various subgroups of patients may be seen in table 3. Six patients (1.29 per cent) were not benefited sufficiently by the program to be able to leave the hospital and continued to need nursing or infirmary type care. Fifty-one patients (10.94 per cent) improved sufficiently to achieve at least partial self care and ambulation, but required domiciliary care either because the family could not provide adequate additional care in the home or the patient had no home to which to return. Twenty-two patients (4.71 per cent) died during the period of rehabilitation due to exacerbation of the initial illness or due to intercurrent illness. Three hundred and eighty-seven patients (83.7 per cent) were able to return home and not be a burden to their families. In each treatment subgroup the percentages are essentially the same as in the total group. The percentages tend to be slightly misleading due to the small size of the individual samples in each subgroup. As would be expected the patients with hemiplegia and extrapyramidal disease contribute the major number of patients who required continued hospital or domiciliary type care.

It will be observed from the statistics that age plays a minor part in influencing the degree of improvement, regardless of the treatment group or of the degree of initial disability in self care or ambulation. It will also be observed that the degree of clinical disability, though the samples are generally too small to make specific statements, does not seriously weigh against improvement in self care and ambulation. In general, even with an initial point score of ability less than 25, 80 per cent of all patients will show improvement and half of these most severely disabled patients will have more than a 75 point score ability in self care and ambulation on discharge. This residual disability will not be sufficient to prevent adequate physical adjustment in the home but may preclude gainful employment.

DISCUSSION

There have been few reports in the literature concerning similar rehabilitation programs. Dinken[2] reported a group of 50 hemiplegic patients with an average age of 62.4 years, 16 per cent of whom were ambulatory on ad-

mission and 94 per cent ambulatory on discharge. The average period of hospitalization was 6.1 weeks. Lowman[3] reported a group more similar to our's, consisting of 28 hemiplegic patients who had eight months of intensive therapy. Eighteen of these patients had been hospitalized for a variable period of time without rehabilitation before beginning the intensive treatment period. The average hospitalization period was 118.5 days; 66 per cent became ambulatory, 17 per cent improved, and 17 per cent were unimproved. In a group of ten patients who had begun treatment during the intensive rehabilitation program, the average hospitalization was 67.1 days; 90 per cent became ambulatory and 10 per cent were improved. The average age for the entire group of 28 was 55.2 years.

In the present group of patients, 47 were transferred to the neurology service as chronic patients who had received only minimum physical therapy or none at all during their previous hospitalization. This group, similar to Lowman's initial group, contributed maximal periods of hospital days for accomplishing recovery on rehabilitation. However, it was felt that a great psychologic factor with dependency upon the hospital was one of the deterrents in making more rapid progress on the rehabilitation program.

It is recognized that a certain number of spontaneous recoveries will occur in the various clinical groups which have been reported. However, the rehabilitation time significantly decreases the period of hospitalization required to achieve the highest level of recovery and greatly decreases the degree of disability at the end of the period of hospitalization. This is important in avoiding the marked feelings of dependence upon the hospital environment that are frequently observed and in decreasing the period of hospitalization and need for chronic hospital care.

The influence of age in achieving adequate self care and ambulation was suprisingly small. The general physical debility accompanying advanced age was, of course, a factor in increasing the time required for maximum rehabilitation and in the final degree of ability, but was not as great as expected on a cursory clinical impression. The degree of initial disability also was not an influential factor in determining the final level of ability. The disease category was the most significant factor.

It is realized that there is a large concomitant psychologic factor in such a program as we have maintained. The entire staff is oriented toward keeping the goal of return to the home environment before the patient, and the social worker maintains this orientation in all her contacts with the family. This is reinforced by the contacts of the physician and the family and with the physician and the patient. Our favorable results would seem to be based on an intensive program of coordinated therapies and a goal-centered program.

It is obvious that the costs of hospitalization are greatly reduced by such a program since the majority of these patients, if past experience is valid, would be considered chronic hospitalization patients with little anticipation of ever leaving the hospital environment.

SUMMARY

1. Rehabilitation of the patient with a chronic neurologic disease requires an integrated program of all departments.

2. Maximum rehabilitation was accomplished in 466 patients in a period averaging about 12 weeks.

3. Even with minimal self care and ambulation ability at the onset of the program, over 80 per cent of the patients will show improvement sufficient to return to their home environment.

4. The type of neurologic disease is the most important factor in the degree of total rehabilitation. Age is a less important factor, except in those over 65 years.

5. The rehabilitation program materially lessens the hospitalization period and greatly decreases the chronic neurologic in-patient load in the hospital.

The author is indebted to Miss June Roberts and Miss Muriel Vanderbilt for aid in tabulating the raw data, and to the department of biometrics of the School of Aviation Medicine, Randolph Air Force Base, Texas, for preparation of the tables.

REFERENCES

1. V. A. Pamphlet 10-29, May 1949.
2. Dinken, H.: Evaluation of disability and treatment in hemiplegia, Arch. Phys. Med. 28:263, 1947.
3. Lowman, E. W.: Rehabilitation of the hemiplegic patient, J.A.M.A. 137:431, 1948.

Convulsions may not only result from active brain disease, but also from brain disease which is no longer in an active state, which has become quiescent, or has even retrogressed, so that merely a cicatrix may be found on post-mortem examination. Such disease may be one which, in its active state, commonly causes convulsions, such as a cerebral tumor. The other symptoms, as headache, optic neuritis, paralysis, may pass away, but the convulsions persist by a continued morbid action of gray matter which was damaged by the irritation of the lesion in its active stage. For instance, a man, who had constitutional syphilis, suffered from convulsions, optic neuritis, and severe headache, and a syphilitic tumor of the brain was diagnosed. The optic neuritis and headache passed away, but the fits persisted, and some time afterwards he died in a series of severe convulsions, killed apparently by their violence. Post-mortem there was found the atrophied remains of a gumma in the under part of the right frontal lobe. In a large number of these cases the convulsions begin locally, and are thus of the character to suggest organic disease. Whether they begin thus or not, the history of the case shows that at the onset there were symptoms of organic disease, and usually makes the nature of the case clear. Frequently also some of the early symptoms persist, as hemiplegic weakness, optic-nerve atrophy such as is produced by neuritis, hemiopia, etc.

W. R. Gowers in *Epilepsy and Other Chronic Convulsive Diseases*, published in 1885.

TREATMENT REVIEW

This section is designed to give prompt publication to the results of reliable studies in therapy, to record newer methods of treatment, and to encourage research in therapy of neurologic disorders.

AUGUSTUS S. ROSE, M.D., *Section Editor*

Treatment of Migraine in Children

Arnold P. Friedman, M.D.

It is prerequisite for the physician who is treating migraine to be able to differentiate this type of headache from others which so closely resemble it. In order to make this differentiation the clinician should understand the underlying physiologic and psychologic mechanisms associated with this syndrome. In addition, of course, a detailed history and thorough examination are essential. The syndrome in children is similar to that in adults, with the expected history of periodicity, aura, unilateral cephalgia, and associated gastrointestinal symptoms. In children, however, the headache is less severe and abdominal complaints are more prominent.

Though migraine in children is diagnosed infrequently, it is a common occurrence in the author's experience. There are several explanations for this incongruity. Subjective signs such as headache are often difficult to elucidate in young children. The headache tends to be less severe and to recur less frequently than in adults.

This report is based on a study of 100 children with migraine observed during the past six years at the Montefiore Hospital Headache Clinic and in private practice. These children ranged in age from three to 15 years. In most instances thorough routine studies, history of the parents, and a variety of ancillary tests such as electroencephalogram, psychologic tests, and psychiatric interviews, were completed.

Three out of four children complained of headache before the age of nine. (In a study of 600 adults with migraine, 35 per cent reported the onset of headaches before 12 years of age.) A history of headaches was noted in 85 per cent of the parents; a family history of epilepsy was not prominent (2 per cent). There were no appreciable differences in incidence in the two sexes. Physical and neurologic examinations were not noteworthy.

Numerous precipitating factors were mentioned which were usually related to emotional stress. In 40 per cent of

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the patients headaches were preceded by either gastric, psychologic, or visual symptoms. These preheadache symptoms frequently overlapped the headache unless they were visual. Visual symptoms usually disappeared before the headache began. It was noted that, as the children grew older, they complained of throbbing and unilateral pain more frequently. The majority of headaches were frontal, temporal, and retro-orbital.

Associated symptoms were gastrointestinal disturbances, photophobia, and a variety of autonomic disturbances including sweating, chilly sensations, pallor, and so on. Frequently these children with migraine had a history weighted with attacks of biliousness, abdominal pain, and vomiting. In some the gastrointestinal symptoms occurred apart from the headache, while in others they occurred as part of the attack.

Well substantiated observations from various sources have demonstrated that in an attack of migraine the following physiologic changes occur.[1,2] An initial vasoconstriction of certain intracranial branches of the internal carotid artery produces visual and possibly other preheadache phenomena. This prodromal period is followed by dilatation and distention of cranial arteries, primarily in the distribution of the external carotid artery. Stimulation of pain-sensitive nerves in and around the dilated vessels by the increased amplitude of pulsation is the presumed cause of the headache. Persistent dilatation results in a rigid and pipe-like state of the vessels. The pain at this stage is a steady ache, replacing the earlier throbbing, pulsating type. During or following the "vascular pain" there is contraction of the neck muscles and "muscle-contraction pain" develops. This spasm of the muscles is a reaction to the initial pain and may outlast it. The initial phase of the headache is due to stimulation of pain endings which lie in or near the walls of the intracranial arteries, whereas the latter or "muscle-pain" is probably the result of either direct stimulation of nerve endings or ischemia of the muscle. Although the immediate cause of pain in migraine is associated with dilatation of cranial arteries, other dynamic or chemical factors must contribute.

Psychologic factors are of great importance in the migraine attack.[3,4] Personality studies have indicated that many patients with migraine are meticulous, neat in appearance, rigid in their thinking, and excessively aggressive toward their environment. It is often noted that they have had considerable insecurity in their earlier life with resulting tensions which are manifested in inflexibility, overconscientiousness, meticulousness, perfectionism, and resentment.[5,6]

It is the author's impression that psychologic factors play an important part in migraine in childhood.[7,8] Fear of failure, disappointment, rejection, fatigue, unusual stimulation, crying, and other anxiety-producing situations were some of the many causes which commonly preceded headache. On days when important school examinations occurred, children frequently had headaches. Seeing movies, watching television, or even attending an athletic event were exciting factors, possibly because of stimulation of an unconscious fantasy rather than fatigue of visual activity. Many children developed headaches during arguments with parents or siblings. Frequently both mother and child developed a migraine episode during an argument with each other. The inability to express or control hostile feelings toward loved ones was certainly a factor in many of the headaches. However, some children had headaches where there was no apparent evidence of hostility-producing sensations.

The children under study were usually of superior intelligence. No one dynamic pattern was present and all types of personalities were seen. There was, how-

ever, a predisposition toward certain personality traits in the group. These consisted of sensitivity, need for approval, cleanliness, thoroughness, and the need to take responsibilities such as school seriously. These children ranked in the upper level of the class and were considered good students, orderly, and reliable by their teachers and parents. Despite satisfactory performance and apparently good ego structure, they commonly had feelings of inadequacy and excessive guilt. Inhibition of aggressive thoughts and actions were found frequently, but not in all cases. In those children in whom hostility was repressed, there was a strong need for approval by parents and teachers. The headache was often, though not always, related to unexpressed hostility toward these authorities. Psychologic tests confirmed these observations.

The personalities of these children were not specific for migraine and were no different from children without symptoms or in those suffering from other disorders. However, almost all who were studied gave some evidence of neurotic symptoms, such as nail-biting (frequent), feeding disturbances, thumb-sucking, hair-pulling, temper tantrums, enuresis, phobias, or frequent nightmares. Nevertheless, in none of the children were these symptoms severe enough to disturb their lives to a serious degree.

TREATMENT

Treatment of migraine in children, as in adults, must be adjusted to the individual patient's needs.[9] In adults a variety of methods have been used and analyzed including pharmacotherapy, psychotherapy, physiotherapy, and surgery. It has been the author's experience that a dual approach using pharmacotherapy and psychotherapy is the most successful method of treating migraine in adults and children. However, the effectiveness of this type of therapeutic approach varies with the patient's personality, the pharmacologic action of the medication, and the physician's orientation toward the problem.

In children it is especially important to de-emphasize any episodic disturbance, such as migraine. Medication in the treatment of an individual attack should only be used when the need for it has been definitely established. Therapeutic emphasis must lie mainly in the field of psychiatry and social adjustment.

Symptomatic relief from migraine headache is obtained by drug therapy, which as in psychotherapy must have flexibility for its keynote. In pharmacologic treatment an attempt is made to interrupt the mechanism producing pain by using a vasoconstrictor such as ergotamine tartrate which, combined with caffeine (Cafergot), has been proved empirically to be the most effective method of therapy. For each attack the average initial oral dose of Cafergot is one tablet (each tablet contains 1 mg. ergotamine tartrate and 100 mg. caffeine) repeated in one-half hour. However, the minimum effective dose must be determined individually for each patient. Age, weight, and individual tolerance are all factors which must be evaluated individually. The importance of administering the medication early in the course of an attack, as well as in adequate doses, cannot be overestimated. The optimal time of administration is in the prodromal period or immediately after onset of the headache.

Side effects of ergotamine tartrate are variable and may include nausea, vomiting, tingling of hands and feet, pains in the abdomen, and other minor discomforts. It is contraindicated in organic heart disease, septic states, and so on.

In a few cases, aspirin is sufficient to produce symptomatic relief if given early in an attack. We occasionally combine a mild sedative with aspirin, thus producing in combination a reduction of

pain threshold, lessening of tension, and moderate sedation. If possible such a combination should react with minimal side effects, allowing the patient to maintain his usual environmental relations. If abdominal pain is prominent the addition of an antispasmodic which can be combined with either Cafergot or aspirin is advised. During recent years innumerable preparations have been recommended for the symptomatic treatment of migraine, including nicotinic acid, Dexedrine, Octin mucate, vitamin B complex, Prostigmin bromide, Carbachol, Priscoline, hypertonic glucose, oxygen, and so on. It is the author's experience that, except in a few isolated cases, such preparations have little value.

Prophylactic therapy is important in reducing the frequency and severity of attacks. Parents are usually able to understand that a migraine attack might be related to emotional stress. However, it must be kept in mind that, while limitation of the child's activities such as parties, irregular sleep, irregular meals, and movies may reduce the frequency of headaches, such restrictions may also create new personality problems. Even during diagnostic investigations we are aware of the necessity of de-emphasizing incapacities produced by the headaches. The parents are instructed to minimize their own headaches in the presence of the child. This is one of the most significant aspects of prophylactic therapy. In some children psychotherapy is suggested, especially when neurotic symptomatology is outstanding or when the headache is frequent and overwhelming. The majority of cases improve as soon as psychiatric investigation is started. Failure of therapy may be the consequence of failure to orient the parents to the child's problems.

At the present time we cannot draw any conclusions as to the prognosis of migraine in children. However, 35 per cent of the headaches in 800 adults observed in our clinic began in childhood. Emphasis on psychologic factors in children with this condition may do much to alter its natural course. A modification of parental attitudes may be the most effective means of reducing the frequency of migraine. When the child's need for self-assertiveness and love is not understood by parents who are rigid and strict in their training, the chances of developing psychosomatic symptoms are much greater. A child brought up in an atmosphere where aggression and independence are curtailed may develop inhibitions and feelings of guilt and inadequacy, which may play a role in migraine as well as in other disorders. In spite of these observations, we cannot predict how many of these children treated with psychotherapy will lose their tendency toward migraine.

REFERENCES

1. Schumacher, G. A., and Wolff, H. G.: Experimental studies on headache: a) Contrast of histamine headache with headache of migraine and that associated with hypertension, b) Contrast of vascular mechanisms in preheadache and headache phenomena of migraine, Arch. Neurol. & Psychiat. 45:199, 1941.
2. Marcussen, R. M., and Wolff, H. G.: Studies on headache, Arch. Neurol. & Psychiat. 63:42, 1950.
3. Fromm-Reichmann, Frieda: Contributions to the psychogenesis of migraine, Psychoanalyt. Rev. 24:26, 1937.
4. Selinsky, H.: Psychological study of the migrainous syndrome, Bull. New York Acad. Med. 15:757, 1939.
5. Friedman, A. P., and Brenner, Charles: Psychological mechanisms in chronic headache, A. Res. Nerv. & Ment. Dis. Proc. 29:605, 1950.
6. Vahlquist, B., and Hackzell, G.: Migraine of early onset, Acta Paediat. 38:622, 1949.
7. Krupp, G. R., and Friedman, A. P.: Migraine in children, Am. J. Dis. Child. 85:146, 1953.
8. Katz, J.; Friedman, A. P., and Gisolfi, Anne: Psychologic factors of migraine in children, New York State J. Med. 50:2269, 1950.
9. Friedman, A. P., and von Storch, T. J. C.: Studies on vascular headache; One thousand cases of migraine and tension headache, South. M. J. in press.

NEWSLETTER

FEBRUARY, 1954

AMERICAN ACADEMY OF NEUROLOGY

Howard D. Fabing, President
Walter O. Klingman, President-Elect
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AAN Officers Meet in New York The Academy officers and board of trustees convened at the Hotel Roosevelt, New York City, for an all-day meeting on December 10, 1953. Principal purpose of the meeting was to review the Academy constitution and bylaws and discuss the need, if any, for its modification or revision in the light of the great growth in membership and the expansion of activities since the Academy's inception in 1948. Other pertinent matters discussed were the printing of a membership roster, a report on the Academy's official journal, NEUROLOGY, and a further clarification of the category of associate membership. These deliberations and recommendations of the officers and board of trustees will be presented to the membership at the annual AAN meeting to be held at the Shoreham Hotel, Washington, D. C., April 26-May 1, 1954.

ARNMD Elects New Officers At the thirty-third annual meeting of the Association of Nervous and Mental Disease, held at the Roosevelt Hotel, New York City (December 11-12, 1953), Dr. Rustin McIntosh, professor of pediatrics at Columbia University College of Physicians and Surgeons, was elected president. Other officers elected were: Dr. Walter O. Klingman, 1st vice-president, and Dr. William S. Langford, 2nd vice-president. Clarence C. Hare and Rollo J. Masselink continue as secretary-treasurer and assistant secretary, respectively. Recently the society has appointed a committee on public relations with Walter O. Klingman serving as chairman....The topic for the 1954 scientific sessions will be "Psychiatry and Neurology of Childhood."

Gay Elected President of Neurosurgical Congress At the third annual meeting of the Congress of Neurological Surgeons in New Orleans (Nov. 12-14, 1953), James R. Gay of White Plains, N. Y. was elected president, succeeding Nathaniel R. Hollister of Dayton, Ohio. Daniel B. Sweeney was elected vice-president and Bland W. Cannon was re-elected secretary-treasurer. I. J. Jackson, Frank Ernest, and Henry Suckle were added to the executive committee....At

this meeting Sir Geoffrey Jefferson of Manchester, England, was the distinguished guest and presented papers on "Changing Ideas on the Integration of the Brain," "Trigeminal Tumors," and "Chismal Gliomas."

Other Annual Meetings At the annual meeting of the Neurosurgical Society of America at Colorado Springs, the following officers were elected: Dr. C. Douglas Hawkes, Memphis, president; Drs. Carl J. Graf, Buffalo, and Charles L. Neill, Jackson, Miss., vice-presidents; Dr. I. Joshua Speigel, Chicago, treasurer; and Dr. Lester A. Mount, New York, secretary....At the annual meeting, Oct. 30-31, in Fort Worth, Texas, the American Academy for Cerebral Palsy chose Dr. Meyer A. Perlstein, Chicago, president, and Dr. Lenox D. Baker, Durham, N. C., president-elect.

* * * * * *

Brown Reports on European Tour Joe R. Brown, of the Mayo Clinic, recently returned from an extensive visit to the neurologic centers in the British Isles and Europe. On the trip he jotted down notes on his experiences and impressions, which he has developed into an interesting travelogue in "walkie-talkie" style. He visited and made rounds in the company of leading neurologists at many of the important centers in England, Scotland, Scandinavia, Switzerland, Germany, and France, eventually reaching Lisbon for the Fifth International Neurological Congress where he felt that his previous tour had served him well in cementing the acquaintances he had made.... After the International Congress, Brown proceeded to Madrid for the Cajal Centennial meeting which was followed by a tour of the Institute where Cajal had done his original work. Here the major social event was a visit to a special farm for the breeding of fighting bulls. Young, gentle bulls were presented for any members of the Congress who wished to try their skill at this classical Spanish sport. Among those who entered the ring for a trial were Michael Brain, and William Scoville, noted neurosurgeon from Hartford, Conn.....Additional highlights of Dr. Brown's report will appear in later issues of the Newsletter.

Livre Jubilaire for Prof. Henri Roger The students and friends of Professor Henri Roger of the Medical Faculty of the University of Marseille and corresponding member of the French National Academy of Medicine are publishing a commemorative volume (livre jubilaire) honoring the occasion of his attaining emeritus status. Among the contributors to the volume are: Alajouanine, Barre, Petit-Dutallis, Tournay, Barraquer Ferre, Van Bogaert, Van Gehuchten, and many other notable European

neurologists....Prof. G. Morin, dean of the Faculty of Medicine and Pharmacy of the University of Marseille, is honorary president of the editorial board.

Wartenberg Invited to Freiburg The Medical Faculty of the University of Freiburg in Baden, in collaboration with the United States Education Commission for Germany in Dusseldorf, has invited Dr. Robert Wartenberg to be guest professor for one year at that university. Dr. Wartenberg was a member of the staff of the Freiburg University until 1935.

* * * * * *

Minnesota Holds Annual Continuation Course The division of neurology of the University of Minnesota held its annual continuation course in clinical neurology for general physicians and specialists at its Center for Continuation Study (January 25-30). Particularly stressed during the sessions were the diagnosis and therapeutic management of the more common neurologic disorders. The guest faculty was composed of several visiting professors of neurology, including Madison H. Thomas, University of Utah College of Medicine; A. Theodore Steegman, the University of Kansas Medical Center; and Adolph L. Sahs, of the State University of Iowa College of Medicine. As is customary, a distinguished scientist gave the annual John B. Johnston lecture as an integral part of the course. This year it was Dr. Andrew T. Rasmussen, professor emeritus of anatomy, University of Minnesota Medical School....This course, which has proved an asset for the practice of neurology in the state of Minnesota, is under the general direction of A. B. Baker, professor and director of neurology, and his staff at the University of Minnesota Medical School, assisted by members of the faculty of the Mayo Foundation.

Training Program at Michigan Expands Completion of the new Outpatient Building of the University Hospital and the recent activation of the new, geographically adjacent VA Hospital has expanded graduate training in neurology under Dr. Russell N. DeJong, professor and chairman of the department at the University of Michigan. The expansion permits an increased number of resident positions and a broader therapeutic experience by providing for a two month rotation of neurologic residents through physical medicine and rehabilitation. The expanded program gives three, and, if desired, four years of residency training. During the first year, three months are spent in basic neurologic laboratories, followed by experience on the neurology wards of the University Hospital where the resident contacts a great variety of neurologic problems and performs such diagnostic

procedures as pneumoencephalography, EEG, and myelography. The second year comprises training in the OPD and responsibility for the supervision of interns and first year residents; during the third year residents are given the responsibility of neurologic consultations and teaching undergraduate medical students.... All residents are encouraged to register in the graduate school for the degree of master of science in neurology.

Briefs Titles and 200-word abstracts for presentation at the next meeting of the Harvey Cushing Society should be in the hands of Program Chairman Dr. Donald D. Matson by March 1. This meeting will be at the La Fonda Hotel, Santa Fe, N. Mex. (May 6-8)....Henry R. Viets was unanimously re-elected chairman of the medical board of the Myasthenia Gravis Foundation at the first annual meeting in N. Y., Dec. 11....Matthew T. Moore has been appointed professor of clinical neurology, Hahnemann Medical College and Hospital (Sept., 1953)....A recent guest lecturer of the National Academy of Sciences and the National Research Council was A. V. Hill, honorary research associate of the University College, London, who lectured on "The Elastic Transition of Muscle From Rest to Activity."....Dr. Robert A. Moore, dean of Washington University School of Medicine, has been appointed vice-chancellor in charge of the schools of the health professions at the University of Pittsburgh, which is engaged in a large medical expansion program....

Percy Bailey

Neurology BOOK REVIEWS

Human Neuroanatomy.

Oliver S. Strong and Adolph Elwyn. Third edition. 1953. Baltimore: The Williams and Wilkins Company. 481 pages. $7.50.

The third edition of this work by the late Oliver S. Strong and Adolph Elwyn of Columbia University continues without essential change from its first and very successful plan. Some additions have been made in the way of further illustrations, and the text has been supplemented by reference to the recent advancement concerning our knowledge of the cerebellum, the thalamus, and in particular of the reticular system of the brain stem.

This treatise sets out to be one thing only: a textbook of neuroanatomy. Its whole orientation is toward the classroom and the laboratory. It is obvious to anyone actively engaged in teaching the subject that the methods of presentation have been tried in the fire of repeated teaching experience. The subjcts are presented in the order in which they are met in the laboratory, proceeding from the spinal cord to the brain stem and thence to the cerebral hemispheres, stopping at each level to identify the structures presented both from the gross specimen and from the prepared section. In this way the textbook is very definitely its own laboratory guide, and this feature appeals most to the teacher. There is no easy way of learning the morphology of any subject; it has to be presented piece by piece in a dissected manner. Thus, the basic value of the book is its recognition that the science of neuroanatomy must be learned in its detached component units.

The authors wisely provide for integration of all this scattered material, and at appropriate places in the text a presentation of a total system is introduced. An excellent example of this is the detailed description of the brain stem. No attempt is being made to conceal the multitude of structures, and yet when they are identified in the laboratory by students, unification into functional systems is provided. Thus each cranial nerve is discussed as a system of anatomic units with its connections with other systems, and a description of its functions and the symptoms which arise from the loss of such functions.

The authors provide an adequate description of the gross anatomy of the nervous system. In those laboratories where good gross material is available, however, the text may need some supplementation. Attention is called to the excellent chapter on the blood supply of the brain. This presents material which is not readily available in textbooks of general anatomy and which is greatly neglected in the teaching of neu-

roanatomy. To the clinician, an accurate description of the blood supply of the spinal cord and brain is of constant importance.

This book, then, may be recommended as an excellent one for teaching the subject of neuroanatomy to undergraduate students, provided that the course intends the discipline of learning the basic units of the central nervous system as they really are to be found by gross dissection and by the study of prepared slides. Its completeness and accuracy are such that it can be recommended as an authoritative reference work.

A. R. V.

Lesion of the Lumbar Intervertebral Disc. With Special Reference to Rupture of the Annulus Fibrosus with Herniation of the Nucleus Pulposus.

R. Glen Spurling, M.D. A Monograph in the American Lectures in Surgery. 1953. Springfield, Illinois: Charles C Thomas, Publisher. 148 pages. $4.75.

As might be expected from the pen of one of the pioneers in disc surgery, this little monograph is a scholarly presentation of the current views of the lumbar intervertebral discs and the syndromes produced by their posterior herniations. The author reviews the interesting history of the disc syndrome to the present concepts introduced by Mixter and Barr, to whom the monograph is dedicated. Brief chapters deal with the anatomy and pathology of the intervertebral disc.

The major part of the book describes clearly and with well selected illustrations the clinical and roentgenologic diagnosis of protrusion of the lumbar discs. Therapy, both conservative and operative, is outlined with particular attention to the details of surgical removal of a herniated disc. Finally Spurling considers the results of therapy on the basis of a long term followup.

This monograph presents the experience of a surgeon who has had a special interest in the problem of intervertebral discs for many years. His views, clearly expressed, are tempered by his extensive clinical contact with his own patients and with those of other neurosurgeons and orthopedic surgeons both in civilian and military practice. Because of this almost unique background, the monograph is particularly interesting. That the author advocates a determined attempt at conservative treatment and a careful evaluation of the case and patient as a whole before surgical intervention is an indication that "the surgical treatment of a ruptured lumbar disc is essentially elective surgery" and not "to be lightly undertaken." The author's advice against operating during periods of remission is also sound judgment. His frank discussion of the operative results of surgery will be welcomed by neurologists. The references appended give a selected list of papers published on the subject and will be useful to students interested in pursuing the problem.

The author has achieved his goal of presenting a simple, concise, and practical account of the lumbar intervertebral disc and the syndromes which result from its posterior herniation. Neurologists, neurosurgeons, and practitioners will find in this beautifully produced monograph frank answers to many questions which have perplexed them.

A. E. W.

Functional Neuroanatomy.

Wendell J. S. Krieg, Ph.D. Second edition. 1953. New York: The Blakiston Company, Inc. 659 pages. 413 illustrations. $9.00.

This is the second and greatly enlarged edition of *Functional Neuroanatomy* by Dr. Wendell J. S. Krieg, professor of anatomy at Northwestern University Medical School. The author has produced a work of real distinction. The field of the structure of the nervous system is described in the traditional manner with, however, constant correlations with functional aspects. The book is designed as a textbook of neuroanatomy for students; with this in mind, it includes laboratory directions and an atlas of sections of the spinal cord and brain stem in the transverse plane, and of the brain in the sagittal, frontal, and horizontal planes.

The characteristic feature of the book is the wealth of illustrations, line drawings done by the author himself or his co-workers, many in three-dimensional perspective, all of which have been drawn especially for this textbook. There is a somewhat leisurely presentation of the subject matter with a certain note of appropriateness of format: the introduction of illuminated letters and other similar touches adds an esthetic quality. In a very practical minded age where drabness is the usual mark of a scientific production, this quality is noteworthy.

Krieg's *Functional Neuroanatomy* will find a place in the libraries, not only of those who are interested in basic neurology, but also of those who collect items of literary value. For this work is presented with such a personal character and such marks of individuality that its inclusion in the category of literature is well justified. A. R. V.

Pain Syndromes. Diagnosis and Treatment.

Bernard Judovich, M.D. and William Bates, M.D. (Foreword by Joseph C. Yaskin). Fourth edition. 1953. Philadelphia: F. A. Davis Company. 440 pages, $7.50.

The popularity of this book on pain is affirmed by the fact that it is now in its fourth edition. In this new edition chapters on the neurosurgical methods of pain control by R. Groff and on vascular pain by S. Lisker have been added, and it is felt that the new viewpoints presented might have been better integrated into the text. For example, in three places in the book (pp. 151, 342, and 410) causalgia is discussed, with three different concepts of the condition and accordingly three methods of treatment.

The descriptions of the various pain symptoms and the methods of symptomatic treatment are quite good. The book will be particularly valuable to general practitioners for it emphasizes the conservative forms of treatment, such as traction for cervical disk, injection of procaine for the scalenus syndrome, and intraspinal alcohol for control of pain in malignancy, rather than operative therapy. The detailed instructions regarding the technic of procaine infiltration of nerves and ganglia should be very useful, especially to those physicians who use the technics only occasionally and do not have the familiarity which comes with everyday practice. One wishes that more consideration might have been

given to the indications for surgical interference for pain.

The illustrations, some 184 in number, are clear and the bibliography well selected. The new edition should continue to be a useful monograph to all physicians and especially to neurologists.

A. E. W.

Personality and the Frontal Lobes. An Investigation of the Psychological Effects of Different Types of Leucotomy.

Asenath Petrie. 1953. New York: The Blakiston Company. pages, $6.00.

In his foreword, David Shakow states, "this investigation has been fortunate both in the kinds of subjects that were available for study and the variety of neurosurgical conditions provided. Previous investigations of 'psychosurgery' have with few exceptions involved psychotic subjects whose prepsychotic and even preoperative personalities were difficult to evaluate objectively and whose postoperative personalities were particularly difficult to extract from the psychotic content." In a neatly designed experiment, Mrs. Petrie has taken full advantage of the availability of an adequate group of adult patients with a disabling neurosis and the opportunity to appraise the psychologic effects of three types of leucotomy: the standard posterior procedure and the open rostral operation, the latter performed bilaterally on one group of patients and unilaterally on certain others.

Without involving herself in elaborate definitions of personality, the author cites differences in temperament and character, as well as intelligence and intellectual functioning. These differences are discussed in terms of performance on certain objective tests relevant to Eysenck's concepts of "neuroticism" and "extraversion-introversion," as well as test scores on the Wechsler-Bellevue scale, omitting the vocabulary and block-design subtests, the Porteus Mazes, and the Meaning of Proverbs item from the Revised Stanford-Binet scale.

All patients subjected to the standard procedure were examined on three occasions, two weeks prior to operation and at approximately three and nine months following it. Their performance is used as a point of reference for the consideration of differences found in the other surgical groups who were tested immediately prior to operation and about six months thereafter. From analysis of these data the author concludes that "with certain reservations the broad statement can be made that the use of objective tests of personality before and after leucotomy enables us to predict the constellation of personality changes following on different types of frontal lobe operations."

Mrs. Petrie presents not only a detailed report of her investigation in both surgical and psychologic aspects, but also a succinct history of the leucotomy operation, a careful description of the objective measures employed, samples of case histories, and examples of the patients' actual productions. All statistical material is presented in an appendix to the volume. In her general discussion the author relates her conclusions strictly to the data reported and most commendably places theoretical implications under the heading "Speculative Possibilities." The organization of this report provides an excellent opportunity for the gathering of comparable data by investigators interested in this field.

C. E. C.

REVIEW COURSES IN BASIC and CLINICAL NEUROLOGY

APRIL 26, 27, 28, 1954

Preceding the

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HEADACHE—April 28, 1954, P.M. Dr. A. P. Friedman, chairman. Fees: Juniors: $5.00; Fellows, Actives and Associates: $8.00; Non-members: $12.00.

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The home is especially designed and fitted for the care of elderly people.

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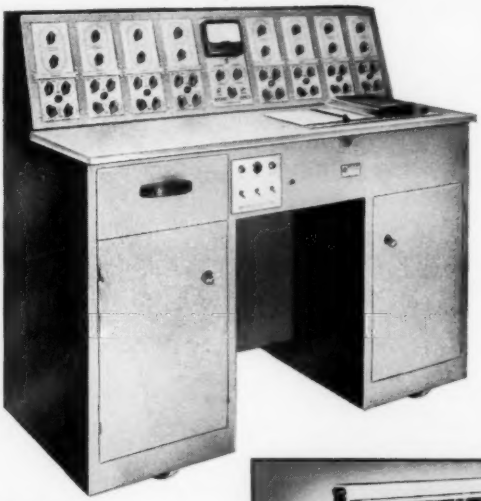

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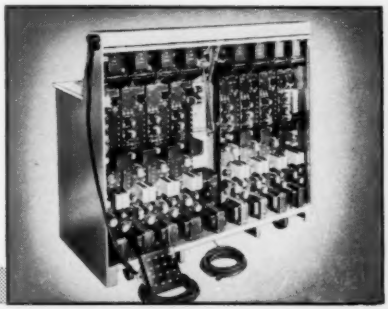

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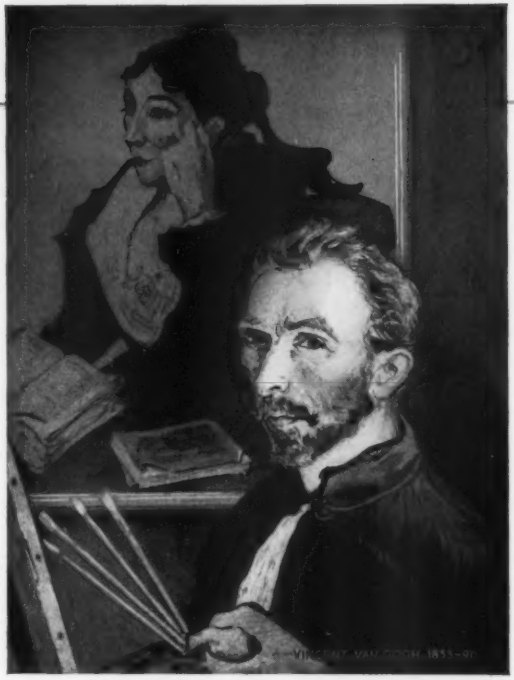

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